Supporting Information for:

Revisiting the 1,3-azadiene-succinic anhydride annulation reaction for the stereocontrolled synthesis of allylic 2-oxopyrrolidines bearing up to four contiguous stereocenters

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Contents:

2. Experimental Section

All experiments involving air and moisture-sensitive reagents were carried out under an inert atmosphere of nitrogen and using freshly distilled solvents. Freshly purchased 1,4-dioxane was stored under 4 A^{o} molecular sieves for several days prior to use. THF was distilled from sodium benzophenone ketyl. All amines, alkenes and enals were newly purchased and used without further purification. Column chromatography was performed on silica gel (230-400 mesh). Thin-layer chromatography (TLC) was performed using Silicycle SiliaplateTM glass backed plates (250 μm thickness, 60 Å porosity, F-254 indicator) and visualized using UV (254 nm) or CAM, *p*-anisaldehyde, or $KMnO_4$ stain. All reported temperatures were internal to a reaction vessel. Unless otherwise indicated, ^{1}H, ^{13}C, and DEPT-135 spectra were acquired using $CDCl_3$ as solvent, at room temperature. Chemical shifts are quoted in parts per million (ppm). HRMS-EI^{+} data were obtained using either electronspray ionization (ESI) or electron impact (EI) techniques. High-resolution ESI was obtained on an LTQ-FT (ion trap; analyzed using Excalibur). High resolution EI was obtained on an Autospec (magnetic sector; analyzed using MassLynx). Brine solutions are saturated solutions of aqueous sodium chloride. The 1,3-azadienes were prepared as previously reported.[1]

General Procedure A: Reaction of 1,3-azadienes with succinic anhydride: A 20 mL screw-cap vial was flame-dried, evacuated and flushed with nitrogen. A solution of the 1,3-azadiene (5.0 mL, 0.10 M in freshly distilled TMO) was added to the vial at room temperature followed by succinic anhydride (500 mg, 5 mmol, 1.0 equiv). The contents were placed in a pre-heated oil bath thermostatted 90 ^{o}C. After complete consumption of the 1,3-azadiene (as judged by TLC, GC-MS, and NMR), the mixture/suspension was cooled to room temperature and washed several times with petroleum ether, then concentrated under reduced pressure to afford the lactam acid.

Methyl esterification of the lactam acid: To a stirring suspension of the acid (1 mmol), dissolved in DMF (5 mL), and K_2CO_3 (414.6 mg, 3 mmol, 3 equiv) was added methyl iodide (0.12 mL, 2 mmol, 2 equiv) under a nitrogen atmosphere. The reaction mixture was stirred for 18 h (TLC monitoring). After complete conversion, it was diluted with water and extracted with EtOAc (3×20 mL). The combined organic extracts were washed with brine, dried over Na_2SO_4 and concentrated *in vacuo* to give the desired ester, which was purified by flash chromatography on silica.

General Procedure B: Halolactonization of lactam acid 3' using catalytic amounts of DMAP

To an oven-dried 10 mL screw-cap vial, equipped with a stir bar, was added lactam-tethered alkenoic acid **3'** (1.0 mmol), dissolved in DCM (5.0 mL). Then, the *N*-halosuccinimide (1.1 mmol,

1.1 equiv) and DMAP (6.1 mg, 5 mol%) were added at 0 ºC. For NIS, the reaction mixture was stirred at this temperature until TLC and GC-MS showed full conversion. For NBS, the reaction mixture was warmed to room temperature and stirred until TLC and GC-MS showed full conversion. For either NBS or NIS, the reaction mixture was then diluted with DCM (20 mL) and quenched with 10% aqueous sodium sulfite (10 mL). The layers were separated and the aqueous layer was extracted once with DCM. The combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated *in vacuo* to give the desired lactam-halolactone, which was purified by flash chromatography on silica.

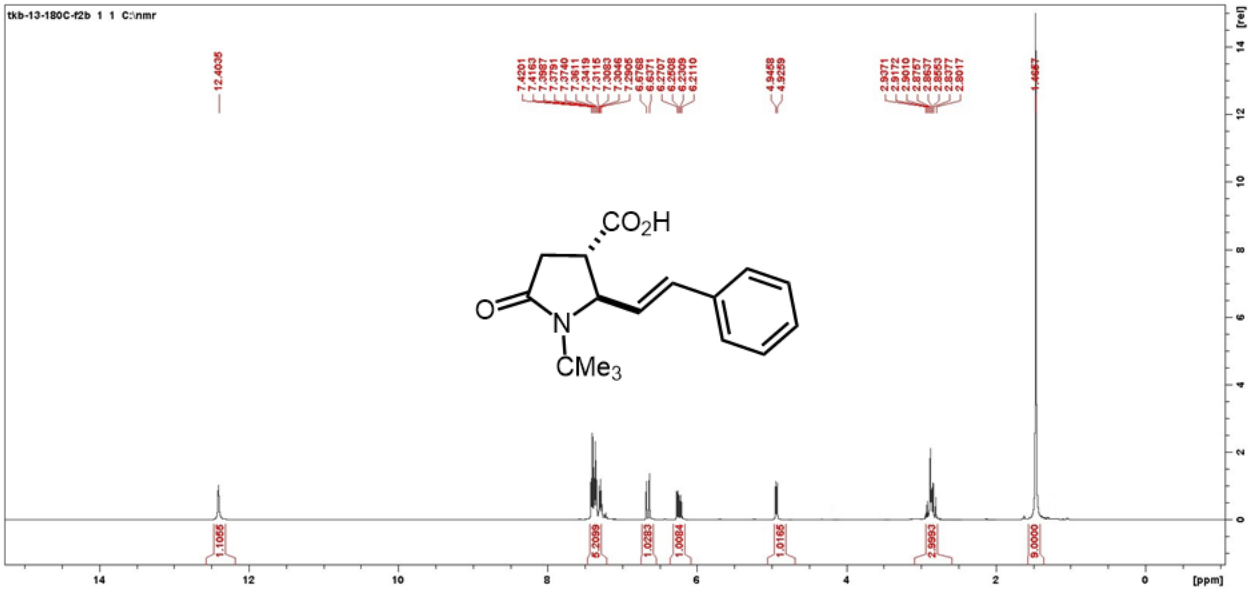
General procedure C: Grignard addition: To a stirred solution of lactam-ester (1.0 mmol, 1.0 equiv) in dry THF (10 mL) cooled to −78 °C, was added a solution of the corresponding Grignard reagent (2.2 mmol, 2.2 equiv) dropwise. After stirring for 10 min at −78 °C, the reaction mixture was warmed to room temperature and stirred for 5 h. After the reaction was complete, as ascertained by GC-MS or TLC, the reaction mixture was quenched with saturated aqueous NH_4Cl, and diluted with EtOAc. The layers were separated and the aqueous later was extracted with EtOAc. The combined organic layers with dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Where it was necessary (most of the Grignard reagents employed in these studies did not require further purification before the next step), flash chromatography on silica gel (hexane/AcOEt) afforded the lactam-tethered alkenols.

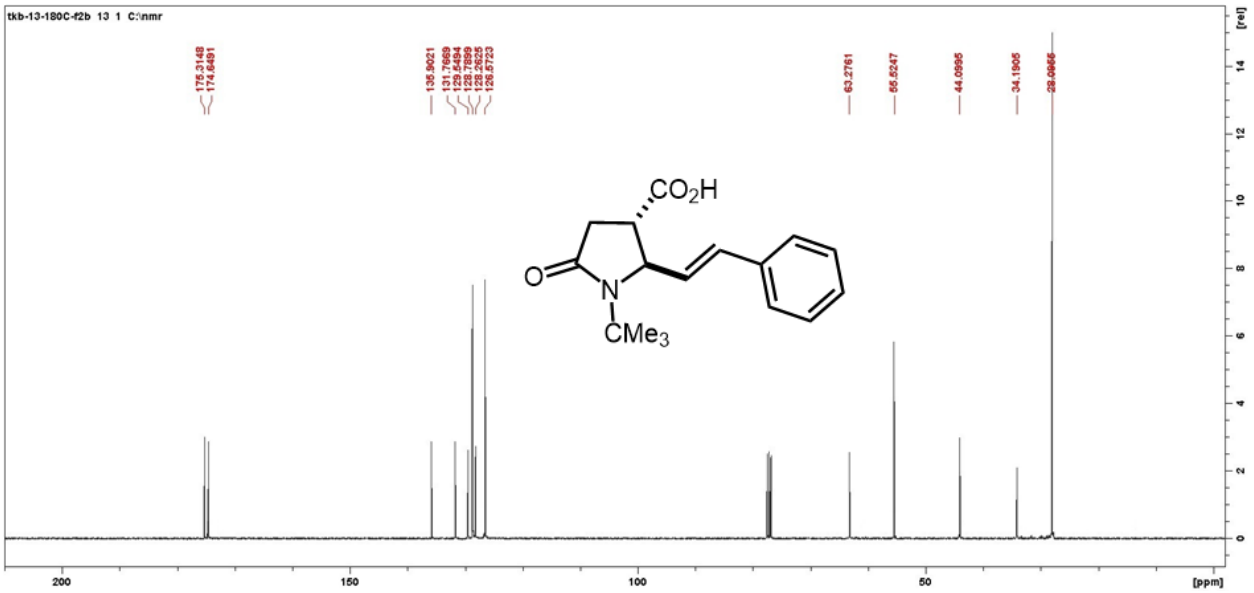
General procedure D: Diastereoselective enolization and trapping with electrophiles: To a stirred solution of lactam alkenol (0.50 mmol, 1.0 equiv) in dry THF (10 mL) cooled to −78 °C, was added dropwise a 1.7 M solution of *tert*-butyllithium in pentane (0.70 mL, 1.2 mmol, 2.2 equiv). After stirring for 15 min at −78 °C, the electrophile (3 equiv) was added, and the reaction mixture was warmed to room temperature and stirred for 18 h. Solid organic halide electrophiles were dissolved in THF prior to the addition to the enolate. After the reaction was complete, as ascertained by GC-MS or TLC, the reaction mixture was quenched with saturated aqueous NH_4Cl and diluted with EtOAc. The layers were separated and the aqueous later was extracted with EtOAc. The combined organic layers with dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Flash chromatography on silica gel (hexane/acetone) afforded the fully substituted lactam alkenols.

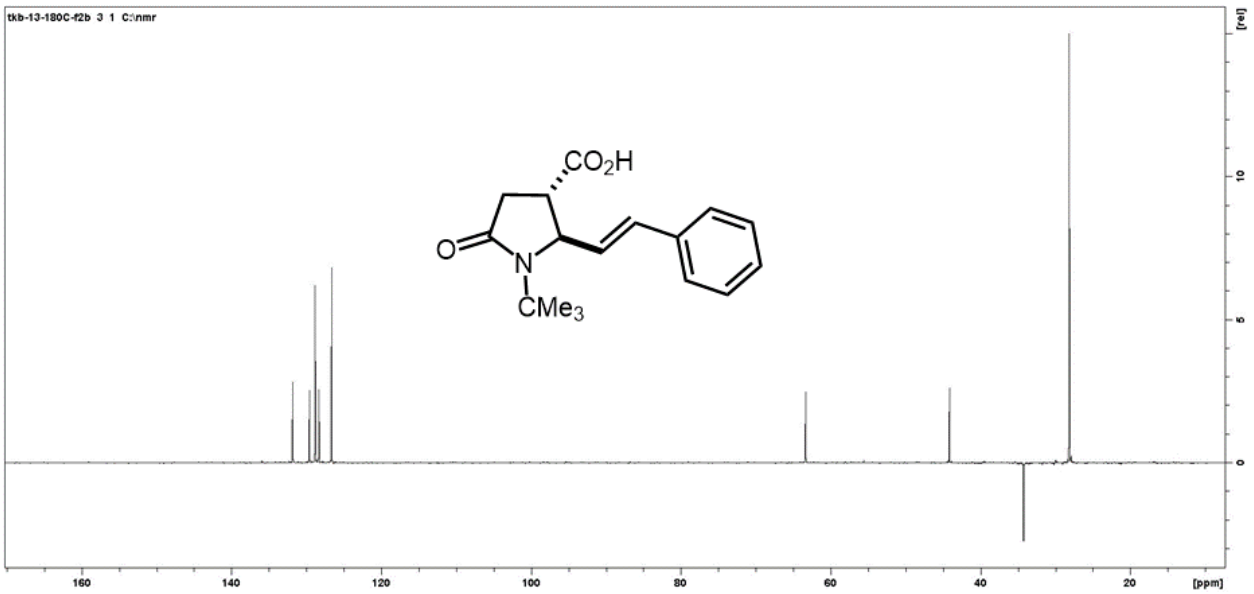
Scheme 1 Results

Compound 3b'

Prepared in 5.0 mmol scale using **General Procedure A** before methylation. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 30:70). Amorphous solid. Yield = 1264.1 mg, 88%, 95:5 dr (*anti:syn*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.40 (s, 1H), 7.44 – 7.18 (m, 5H), 6.56 (d, J = 15.9 Hz, 1H), 6.26 (dd, J = 15.9, 7.8 Hz, 1H), 4.94 (dd, J = 7.8, 1.0 Hz, 1H), 2.97 – 2.78 (m, 2H), 1.46 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.32, 174.65, 135.91, 131.77, 129.55, 128.79, 128.27, 126.58, 63.28, 55.53, 44.10, 34.19, 28.10. **HRMS-EI^{+}** (*m/z*): calc for $C_{17}H_{21}NO_3$ $[M]^{+}$ 287.1521, found 287.1527. FTIR (KBr): 3201.3, 3022.1, 2972.9, 1721.1, 1667.7, 1628.3, 1495.3, 1448.2, 1395.1, 1364.2, 1202.9, 1141.9, 965.6, 741.3, 692.1.



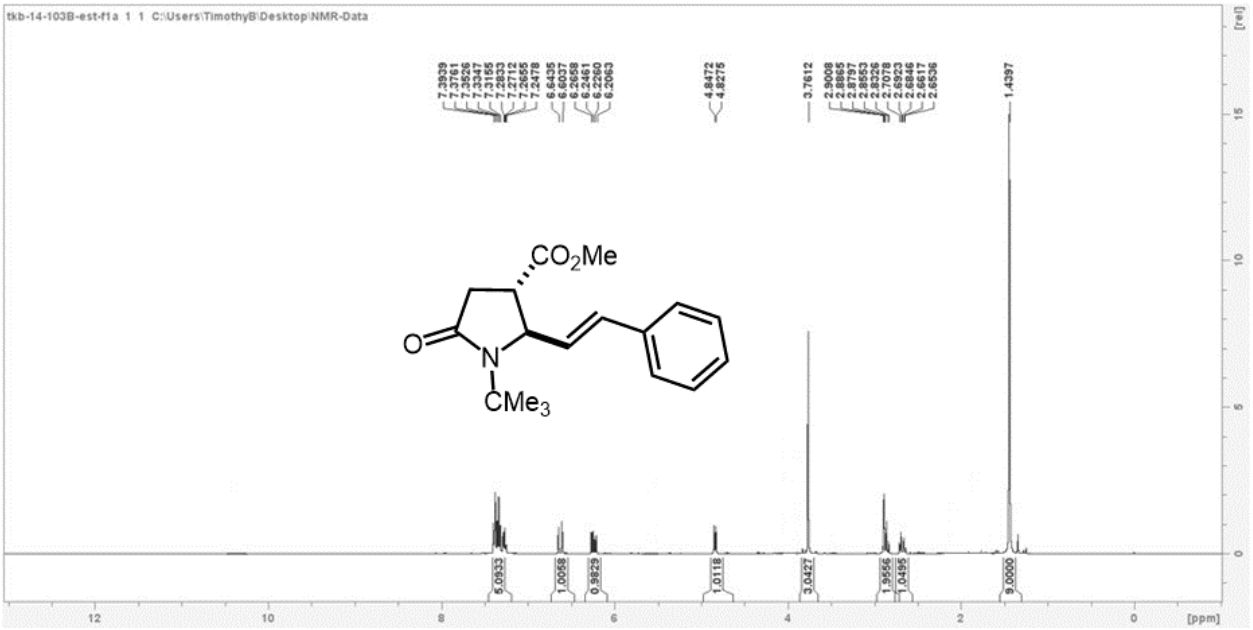


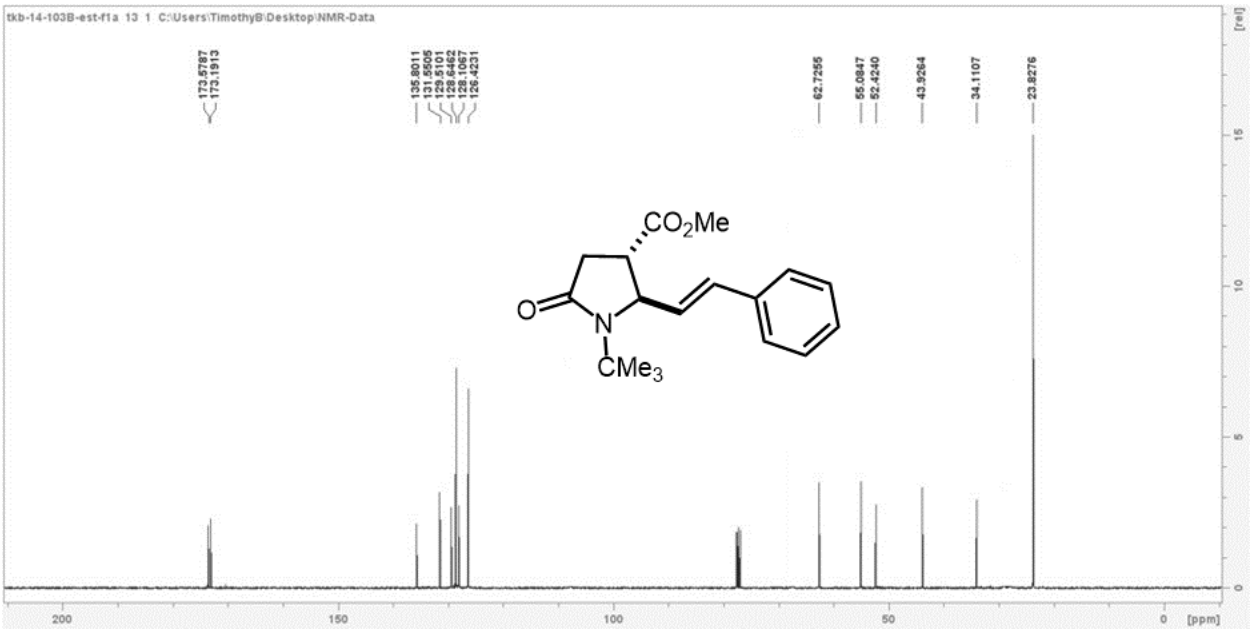


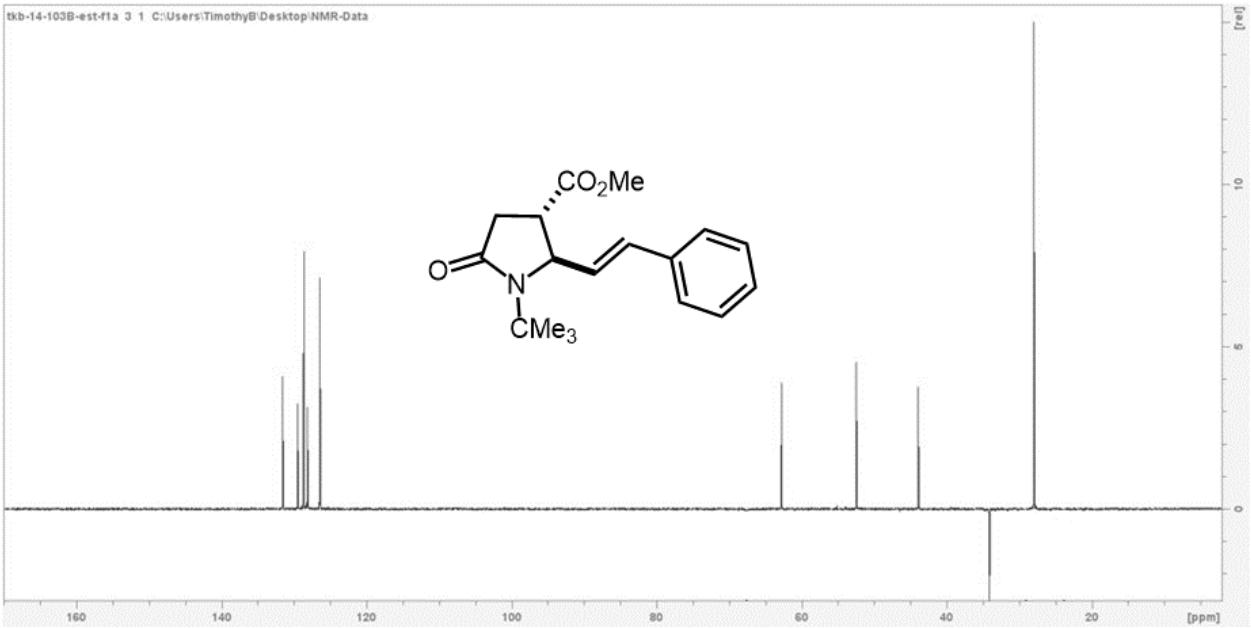
Compound 3b

Prepared in 1.0 mmol scale using **General Procedure A**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 70:30). Yellowish oil. Yield = 259.2 mg, 86%, 95:5 dr (*anti:syn*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.24 (m, 5H), 6.62 (d, *J* = 15.9 Hz, 1H), 6.22 (dd, *J* = 15.9, 7.8 Hz, 1H), 4.83 (dd, *J* = 7.8, 1.0 Hz, 1H), 3.76 (s, 3H), 2.90 – 2.83 (m, 2H), 2.71 – 2.65 (m, 1H), 1.44 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.20, 172.88, 135.94, 131.53, 129.87, 128.83, 128.81, 128.27, 126.62, 126.56, 62.59, 54.99, 52.55, 44.11, 34.33, 28.22, 28.17.

FTIR (KBr): 2965.4, 1727.5, 1696.3, 1604.9, 1511.0, 1448.5, 1414.7, 1384.9, 1357.4, 1298.7, 1247.5, 1179.3, 1135.9, 1031.8, 905.8, 839.0. **HRMS-EI**$^+$ (*m/z*): calc for $C_{18}H_{23}NO_3$ $[M]^+$ 301.1678, found 301.1682.



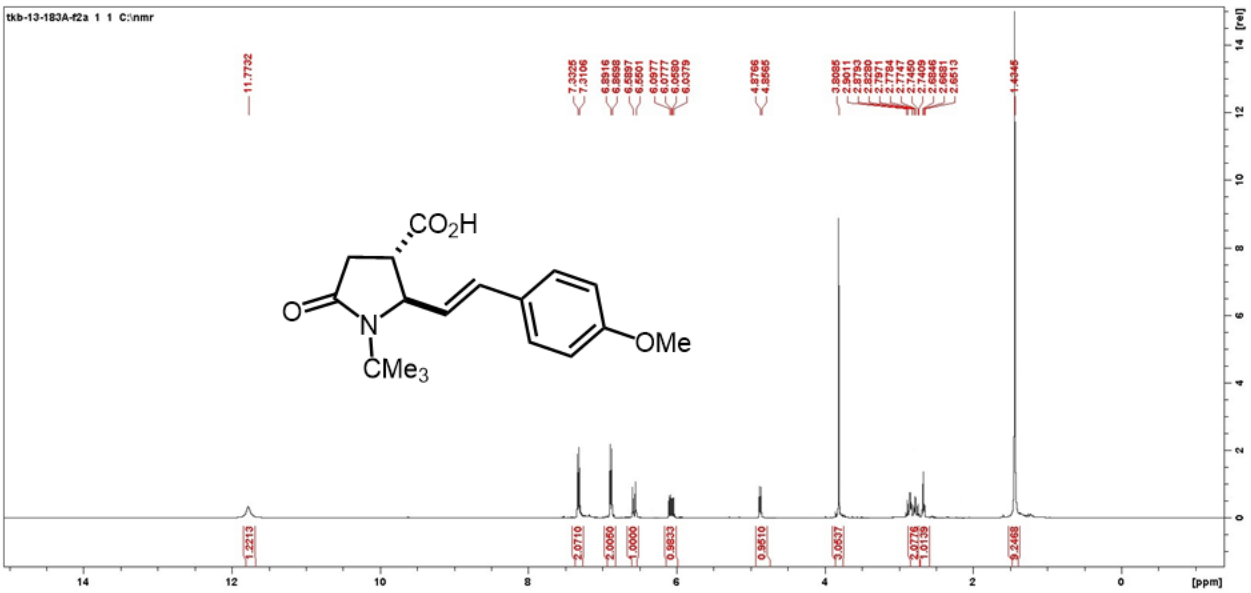


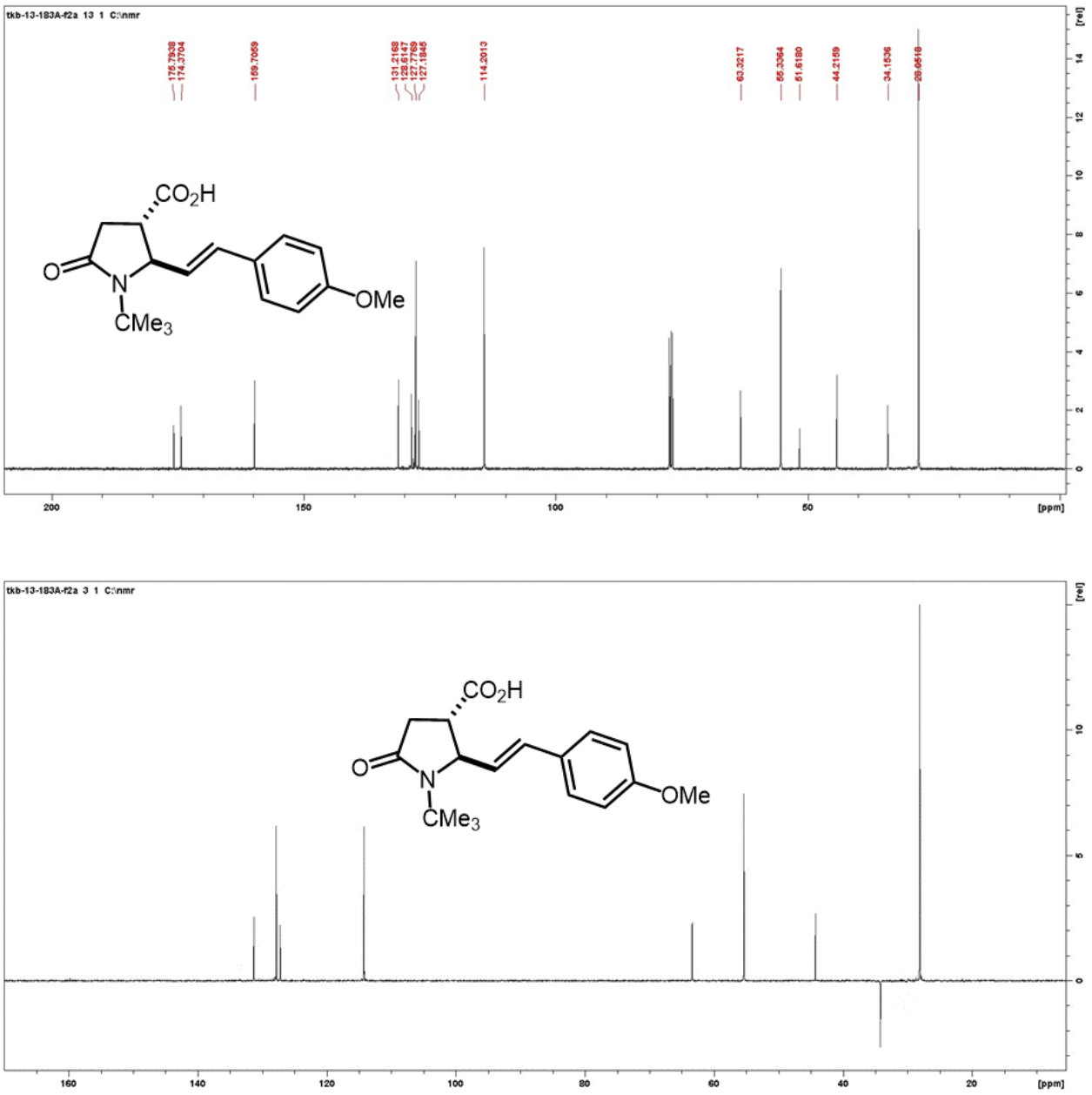


Compound 3c

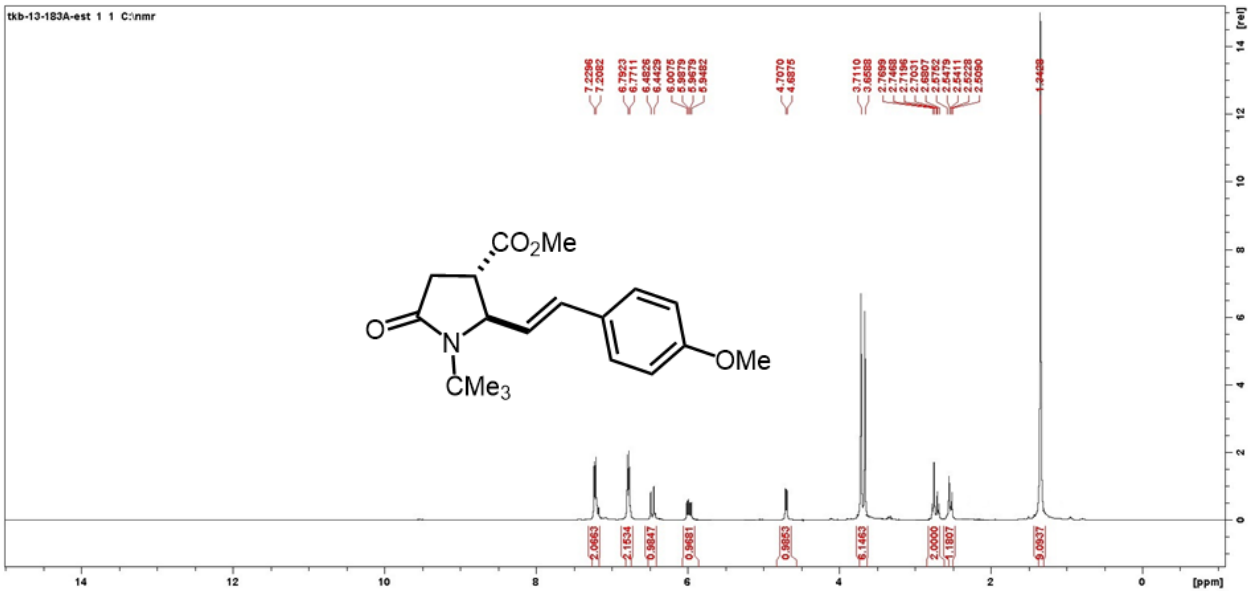
Prepared in 1.0 mmol scale using **General Procedure A**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 50:50). Yellowish oil. Yield = 298.3 mg, 90%, 95:5 dr (*anti:syn*).

Data for the acid (**3c'**): ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.77 (s, 1H), 7.31 (d, J = 2.0 Hz, 2H), 6.89 (d, J = 2.0 Hz, 1H), 6.56 (d, J = 15.9 Hz, 1H), 6.03 (dd, J = 15.9, 8.5 Hz, 1H), 4.87 (d, J = 8.5 Hz, 1H), 3.81 (s, 3H), 2.92 – 2.70 (m, 2H), 2.66 (d, J = 6.7 Hz, 1H), 1.43 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.79, 174.37, 159.71, 131.22, 128.62, 127.78, 127.19, 114.20, 63.33, 55.42, 55.34, 51.62, 44.22, 34.16, 28.06.





Data for the methyl ester (**3c**): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (d, J = 8.3 Hz, 2H), 6.78 (d, J = 8.3 Hz, 2H), 6.43 (d, J = 15.8 Hz, 1H), 5.98 (dd, J = 15.9, 7.9 Hz, 1H), 4.70 (d, J = 7.9 Hz, 1H), 3.68 (s,s, 6H), 2.76 – 2.66 (m, 2H), 2.60 – 2.49 (m, 1H), 1.34 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.16, 172.74, 159.66, 130.90, 128.59, 127.67, 127.48, 114.14, 114.12, 62.66, 55.27, 54.83, 52.36, 44.19, 34.22, 28.06. **HRMS-EI^{+}** (*m/z*): calc for $C_{19}H_{25}NO_4$ $[M]^{+}$ 331.1874, found 331.1879.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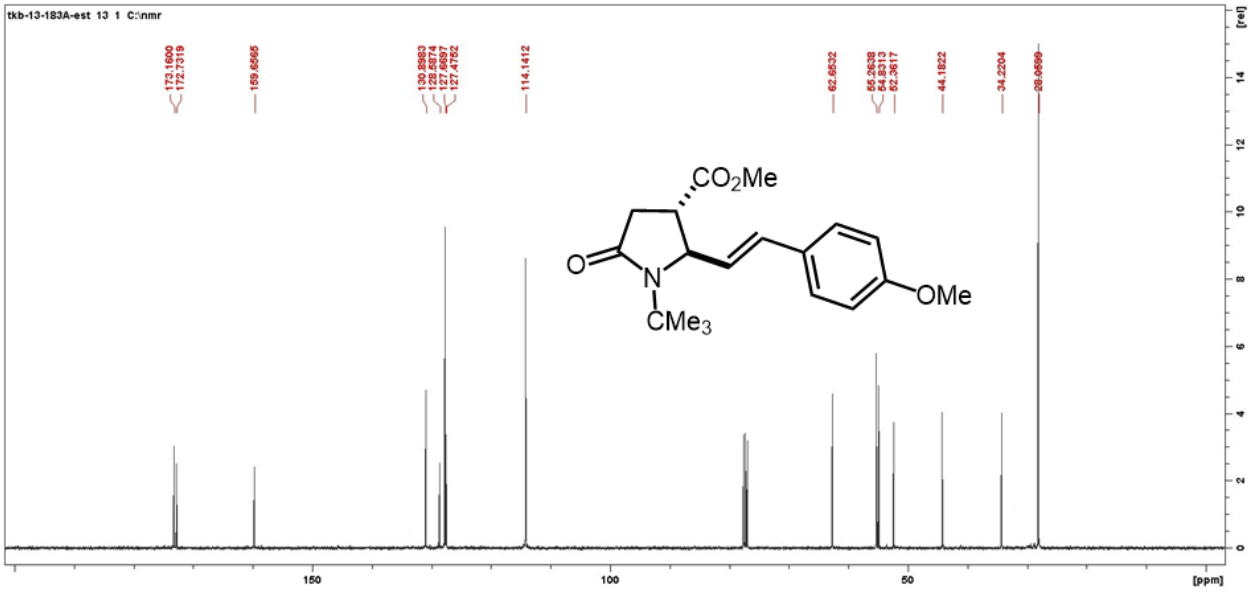
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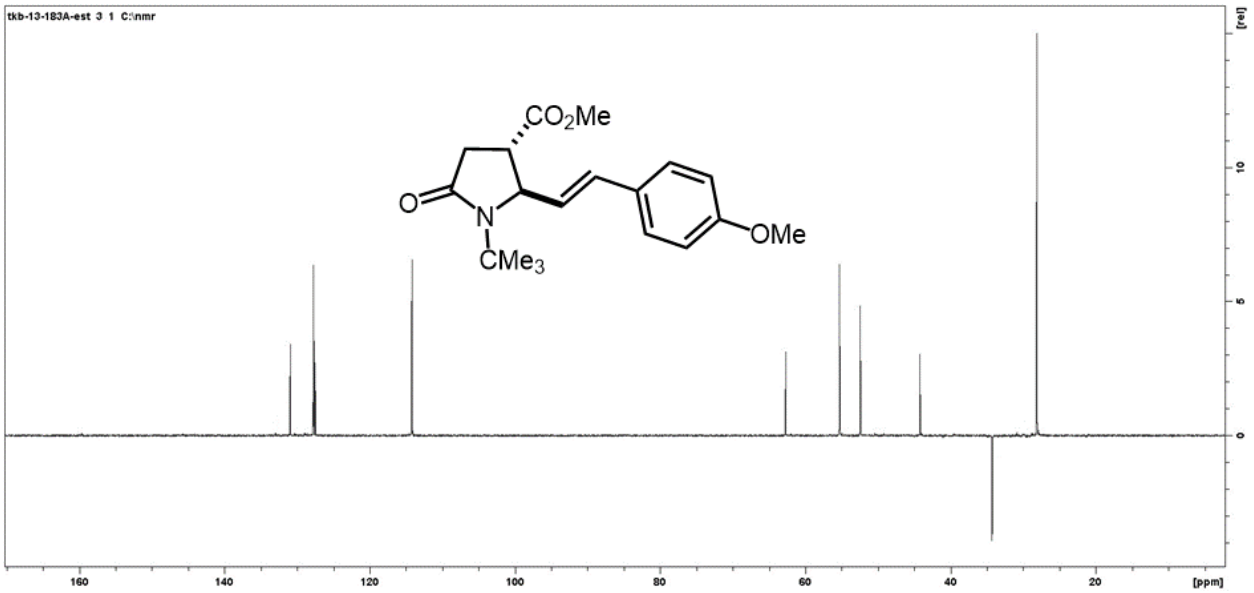
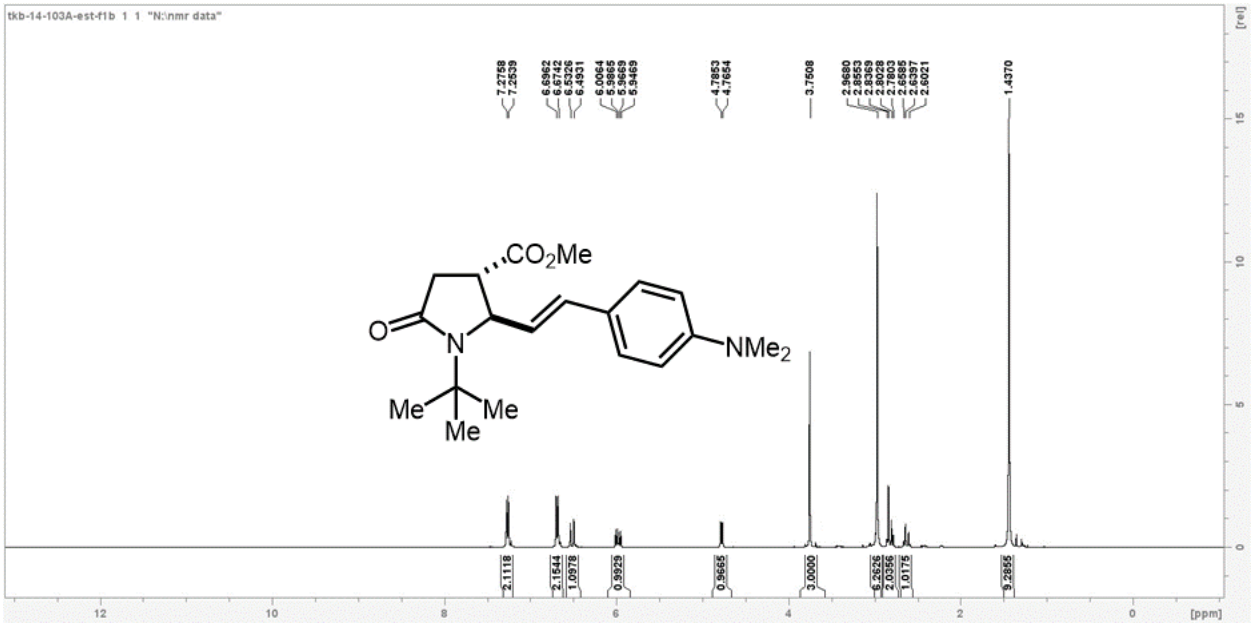
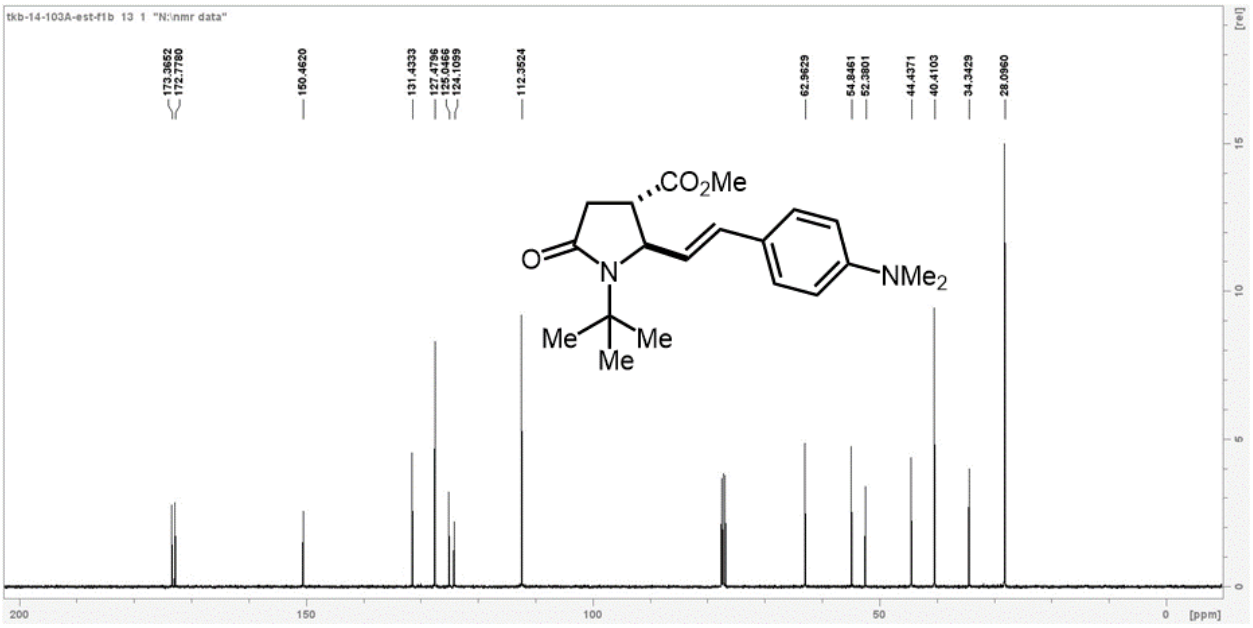
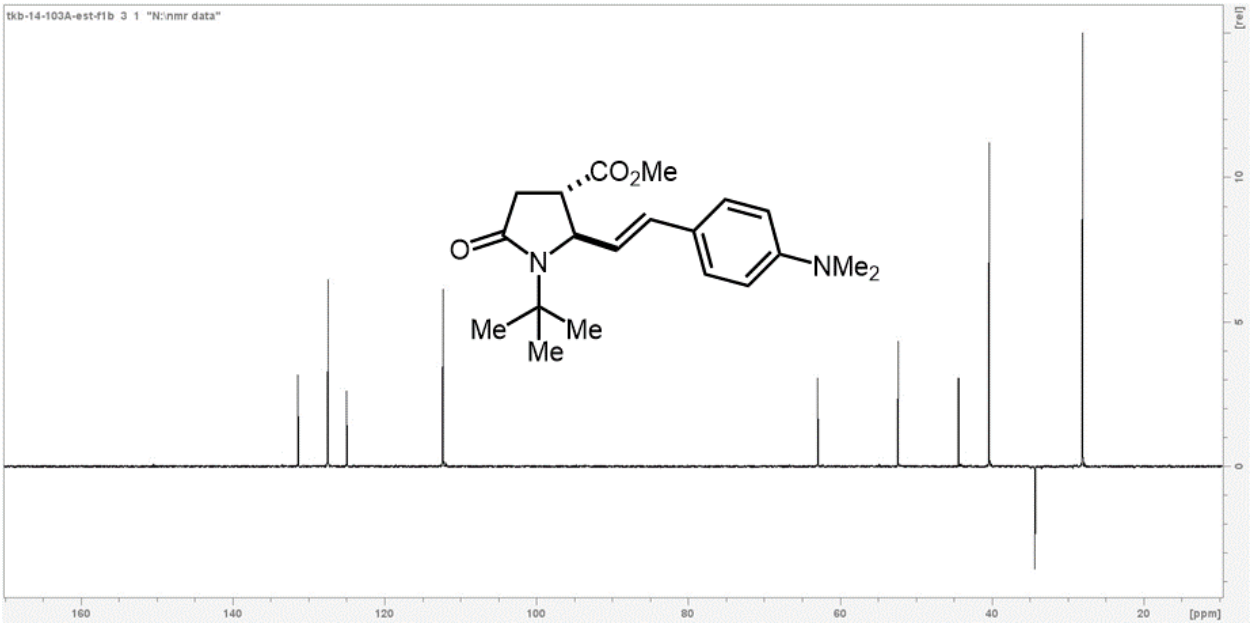


Compound 3d

Prepared in 1.0 mmol scale using **General Procedure A**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 40:60). Yellowish oil. Yield = 320.3 mg, 93%, 95:5 dr (*anti:syn*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (d, *J* = 8.0 Hz, 2H), 6.68 (d, *J* = 8.0 Hz, 2H), 6.56 (d, *J* = 15.8 Hz, 1H), 5.98 (dd, *J* = 15.8, 8.0 Hz, 1H), 4.78 (d, *J* = 8.0 Hz, 1H), 3.75 (s, 3H), 2.97 (s, 6H), 2.88 – 2.76 (m, 2H), 2.68 – 2.56 (m, 1H), 1.44 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.37, 172.78, 150.47, 131.44, 127.48, 125.05, 124.11, 112.36, 62.97, 54.85, 52.38, 44.44, 40.41, 34.35, 28.10. **HRMS-EI$^+$** (*m/z*): calc for $C_{20}H_{28}N_2O_3$ $[M]^+$ 344.2100, found 344.2104.



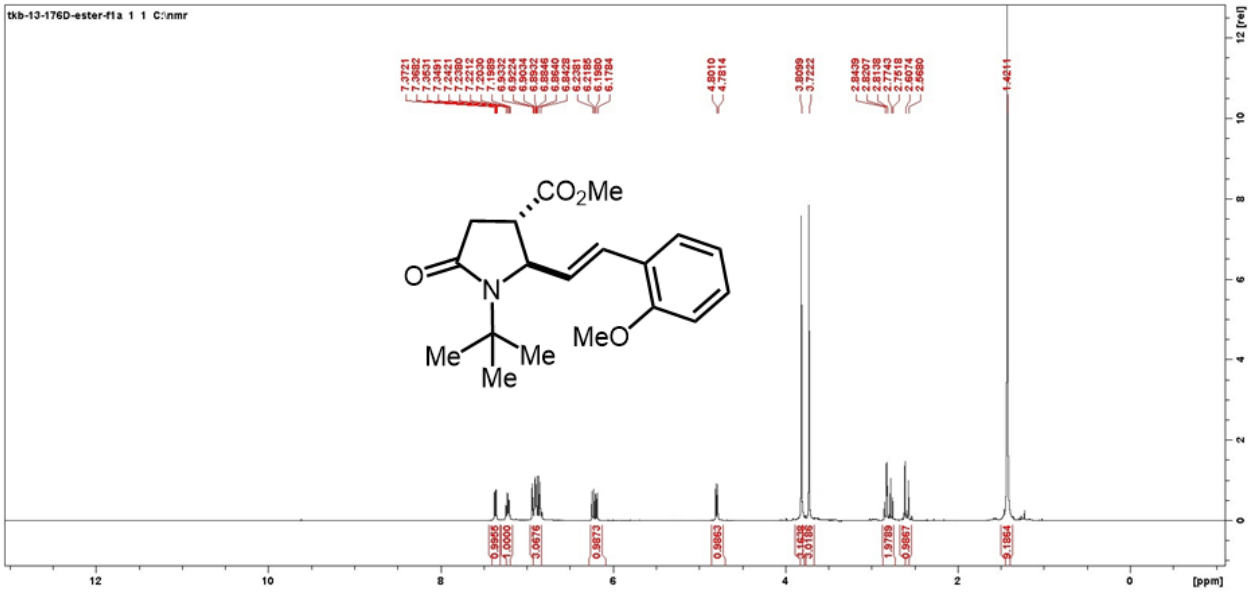


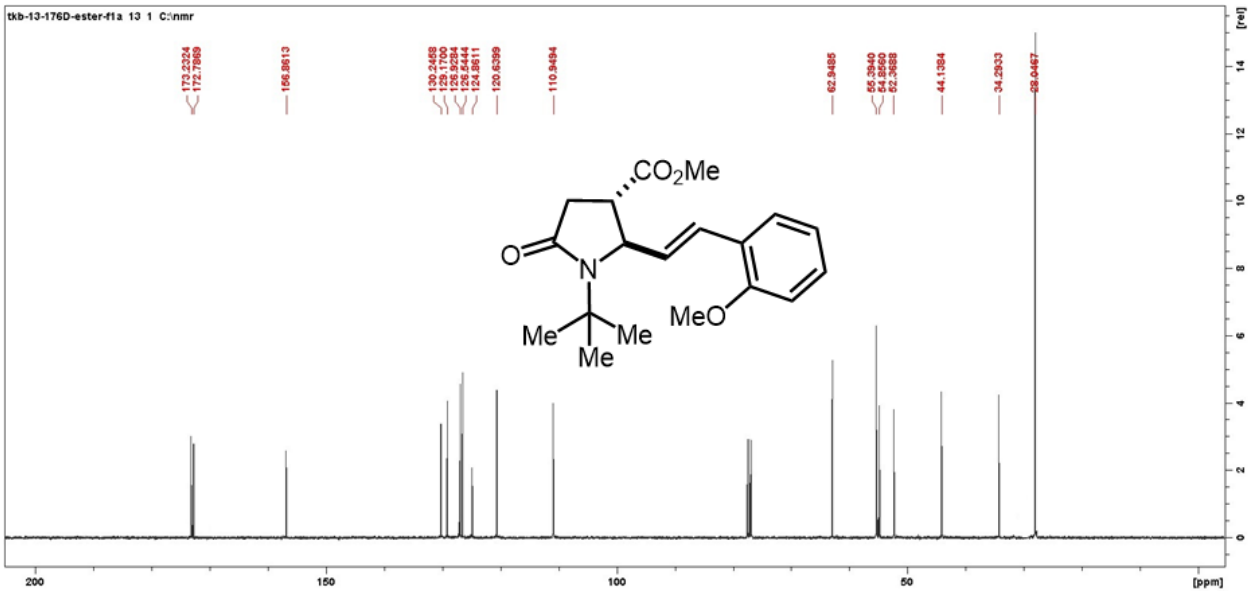


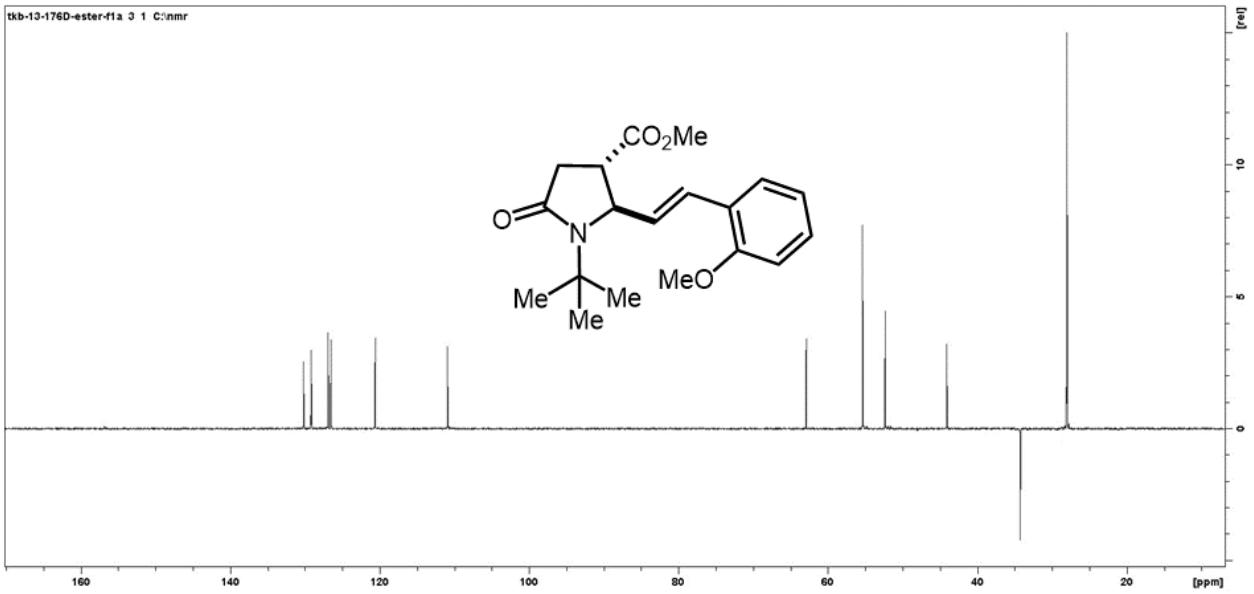
Compound 3e

Prepared in 1.0 mmol scale using **General Procedure A**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 50:50). Yellowish oil. Yield = 265.1 mg, 80%, 95:5 dr (*anti:syn*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.25 (m, 1H), 7.25 – 7.17 (m, 1H), 6.96 – 6.80 (m, 3H), 6.21 (dd, *J* = 16.1, 7.8 Hz, 1H), 4.79 (dt, *J* = 7.8, 1.1 Hz, 1H), 3.81 (s, 3H), 3.72 (s, 3H), 2.87 – 2.73 (m, 2H), 2.66 – 2.55 (m, 2H), 1.42 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.24, 172.79, 156.87, 130.25, 129.17, 126.93, 126.55, 124.87, 120.64, 110.95, 62.95, 55.40, 54.86, 52.37,

44.14, 34.30, 28.05. FTIR (KBr): 2932.4, 1721.5, 1666.3, 1606.9, 1511.0, 1448.5, 1414.7, 1384.9, 1357.4, 1298.7, 1247.5, 1179.3, 1135.9, 1031.8, 995.8, 831.0, 750.2, 694.7. **HRMS-EI**$^{+}$ (*m/z*): calc for $C_{19}H_{25}NO_4$ $[M]^{+}$ 331.1874, found 331.1879.



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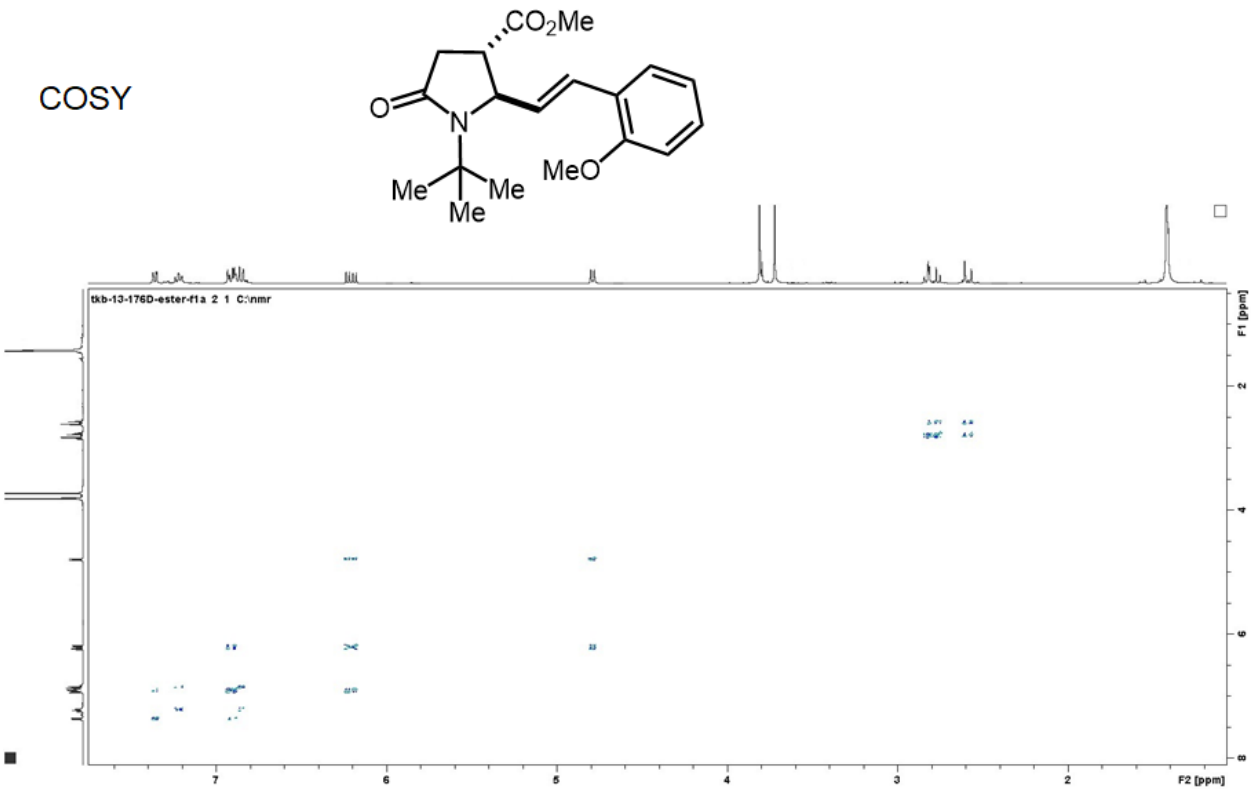
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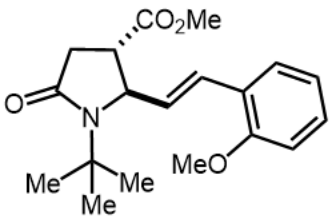

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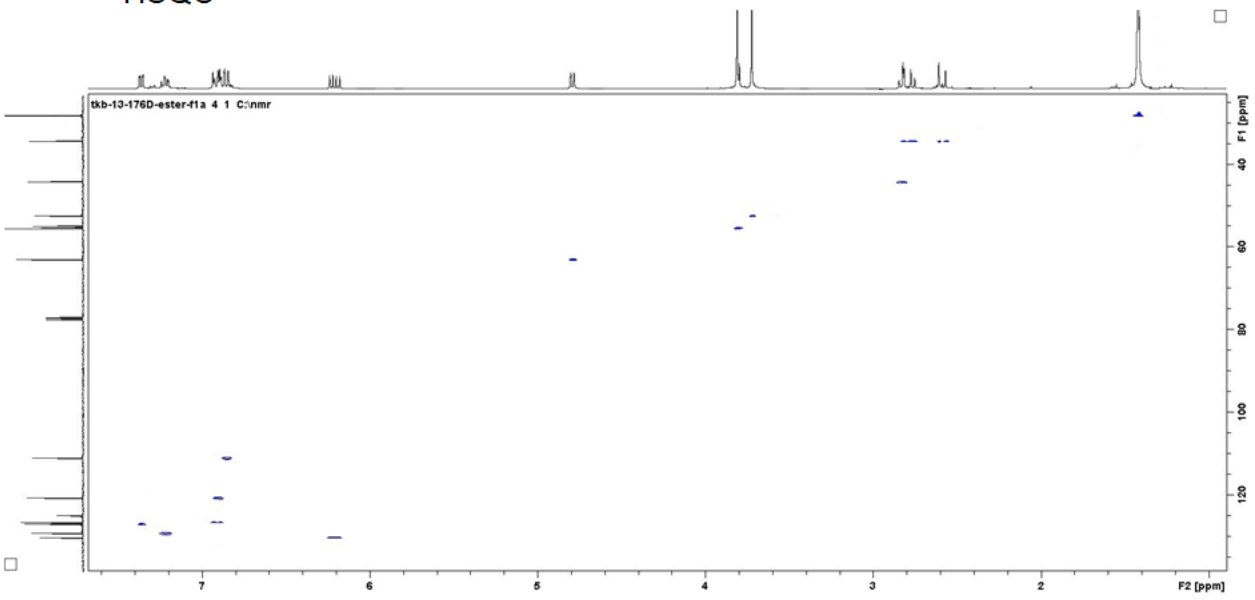
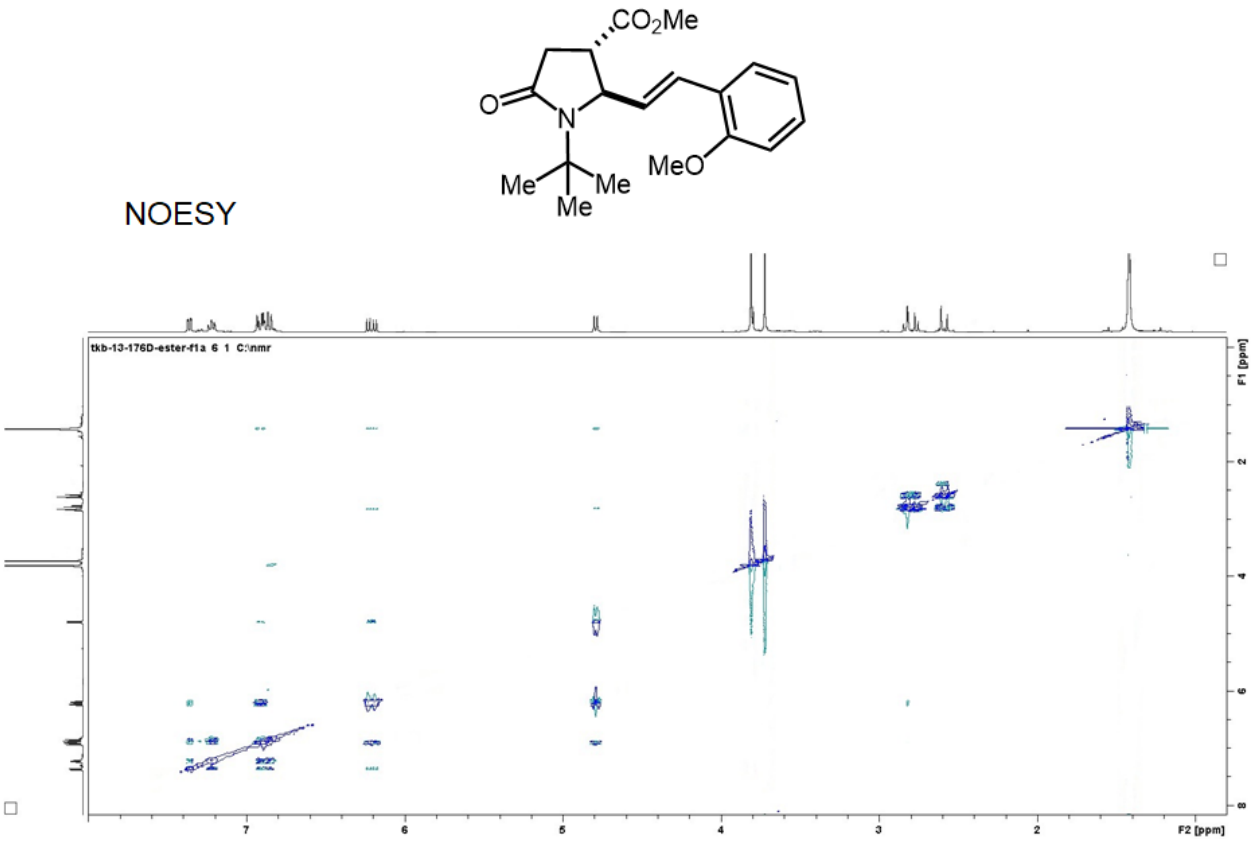
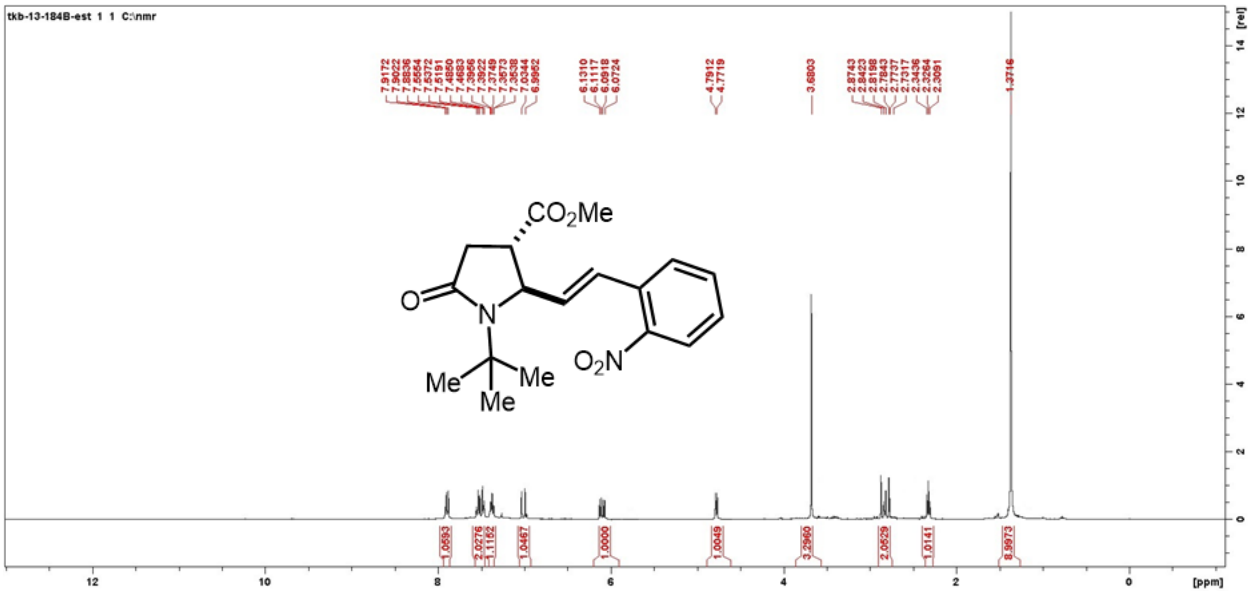




Compound 3f

Prepared in 1.0 mmol scale using **General Procedure A**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 30:70). Amorphous solid. Yield = 218.2 mg, 63%, 95:5 dr (*anti:syn*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 – 7.86 (m, 1H), 7.58 – 7.44 (m, 2H), 7.38 (ddd, J = 9.8, 6.1, 1.7 Hz, 1H), 6.99 (d, J = 15.7 Hz, 1H), 6.10 (dd, J = 15.7, 7.7 Hz, 1H), 4.78 (d, J = 7.7 Hz, 1H), 3.68 (s, 3H), 2.98 – 2.69 (m, 2H), 2.43 – 2.29 (m, 1H), 1.37 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.81, 172.72, 147.62, 135.05, 133.41, 131.99, 128.95, 128.72, 127.38, 124.67, 62.18, 54.99, 52.48, 43.68, 34.15, 28.08. **HRMS-EI$^+$** (*m/z*): calc for $C_{18}H_{22}N_2O_5$ $[M]^+$ 346.1529, found 346.1533.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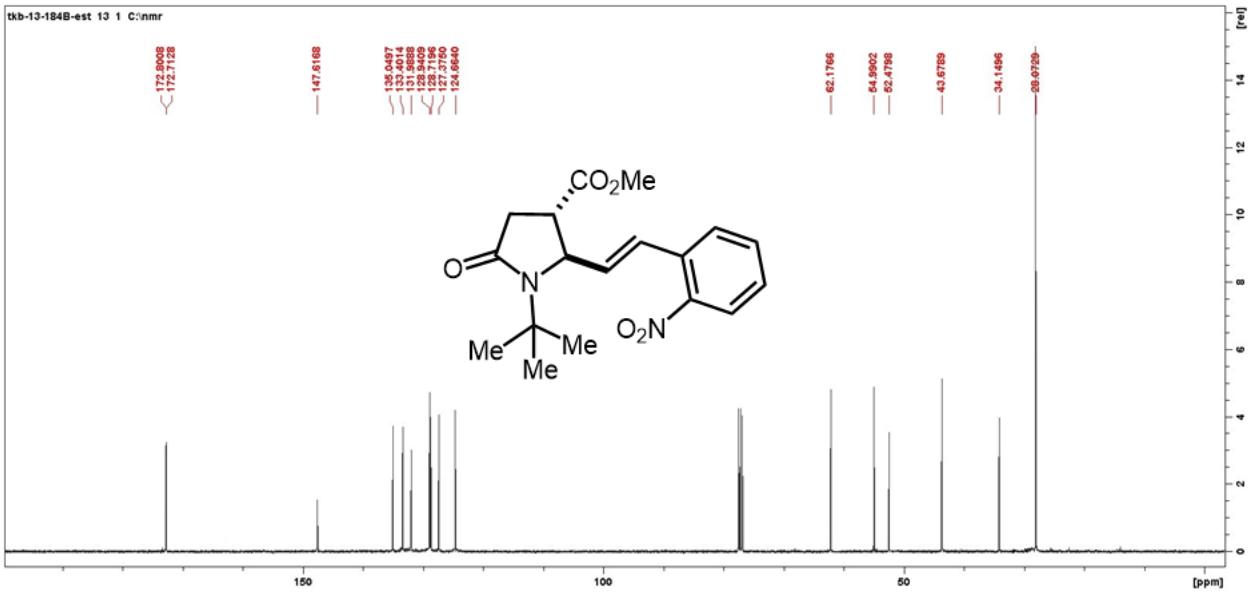
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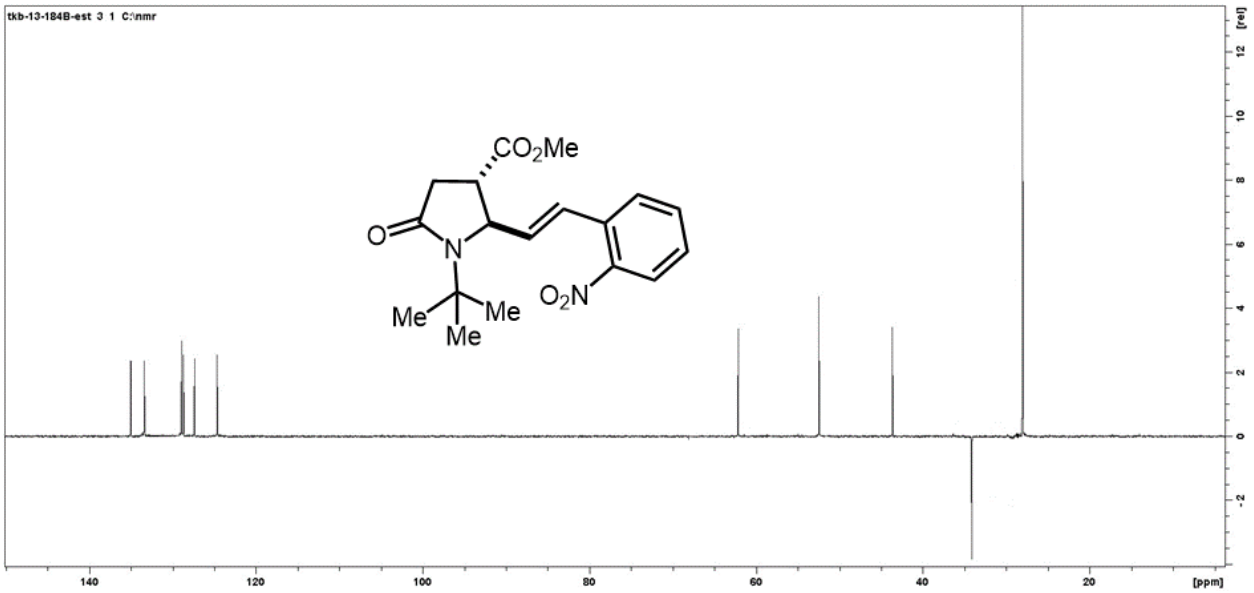
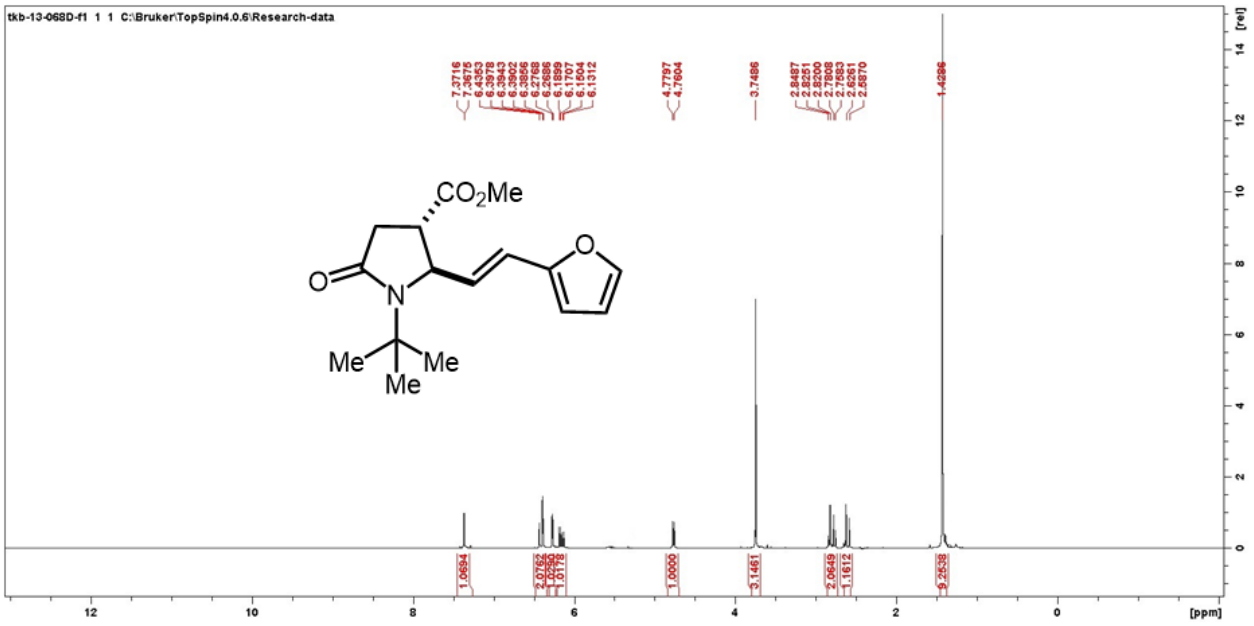
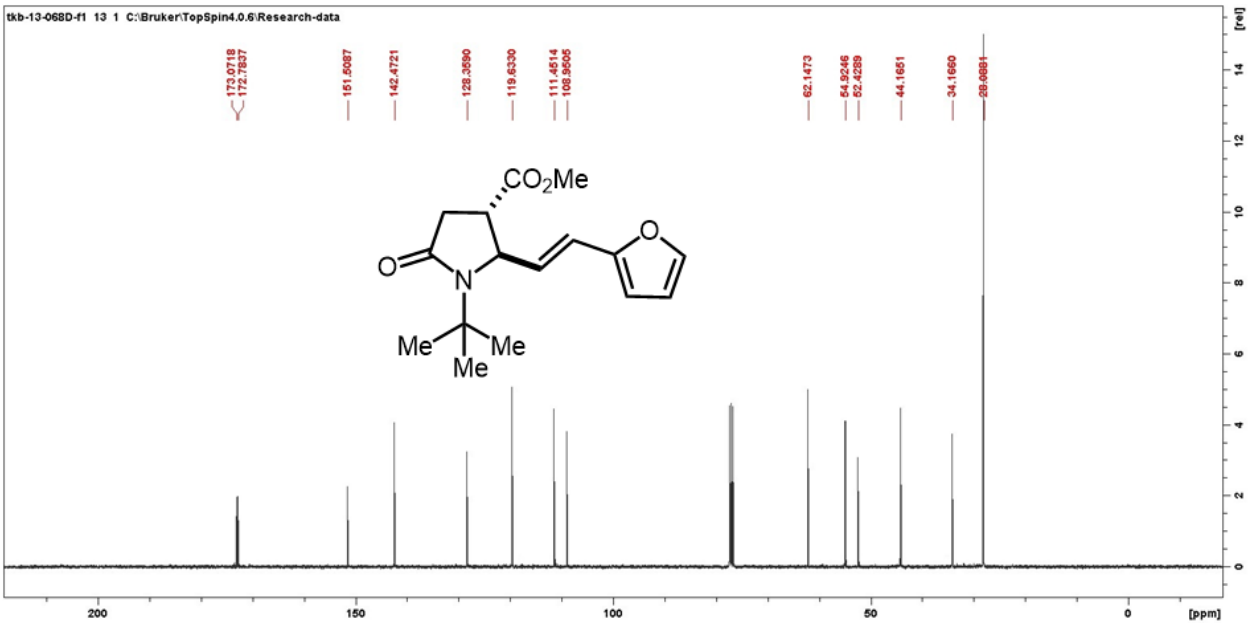
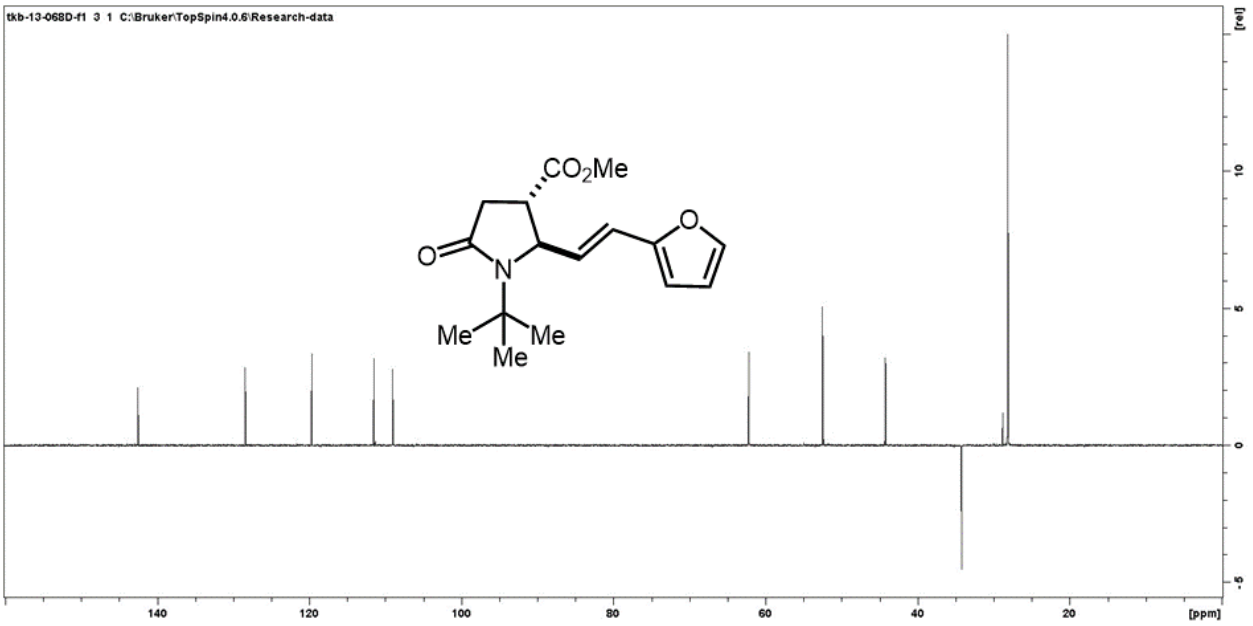


Compound 3g

Prepared in 1.0 mmol scale using **General Procedure A**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 50:50). Amorphous solid. Yield = 259.3 mg, 89%, 95:5 dr (*anti:syn*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, *J* = 7.7 Hz, 1H), 6.43 – 6.38 (m, 2H), 6.27 (d, *J* = 8.2 Hz, 1H), 6.15 (dd, *J* = 15.7, 7.7 Hz, 1H), 4.77 (d, *J* = 7.7 Hz, 1H), 3.75 (s, 3H), 2.85 – 2.75 (m, 2H), 2.63 – 2.59 (m, 1H), 1.43 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.1, 172.8, 151.5, 142.5, 128.4, 119.6, 111.4, 108.9, 62.1, 54.9, 52.4, 44.2, 34.2, 28.1. **HRMS-EI^{+}** (*m/z*): calc for $C_{16}H_{21}NO_4$ $[M]^{+}$ 291.1471, found 291.1477.



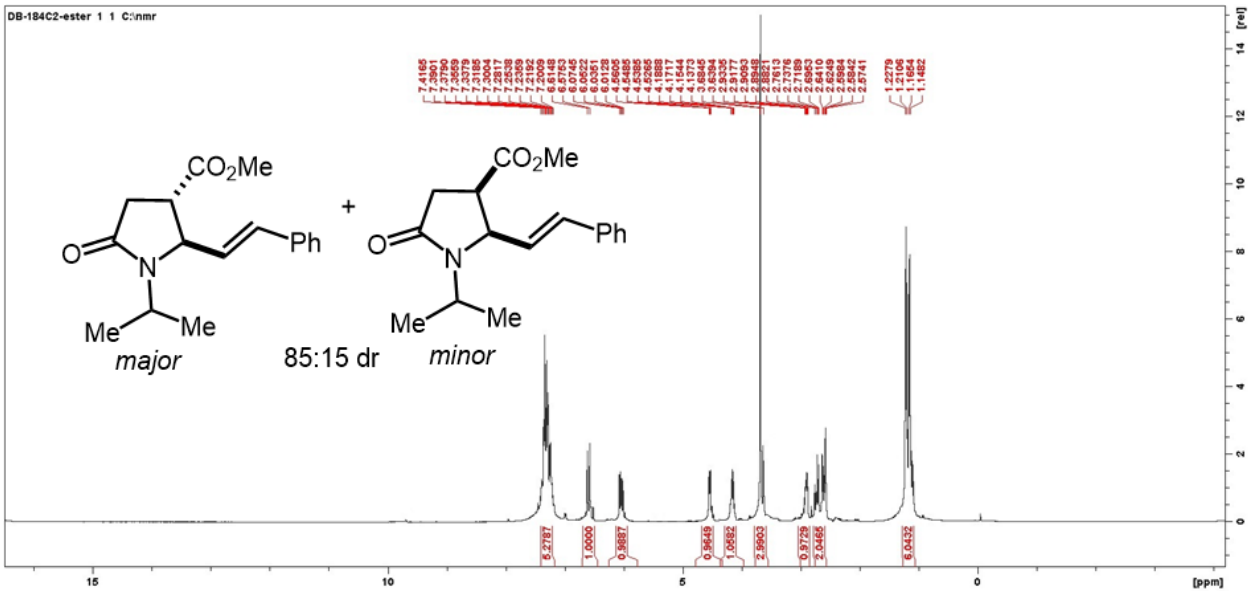




Compound 3h

Prepared in 1.0 mmol scale using **General Procedure A**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 50:50). Yellowish oil. Yield = 218.4 mg, 76%, 85:15 dr (*anti*:*syn*).

HRMS-EI$^+$ (*m/z*): calc for $C_{17}H_{21}NO_3$ $[M]^+$ 287.1521, found 287.1526.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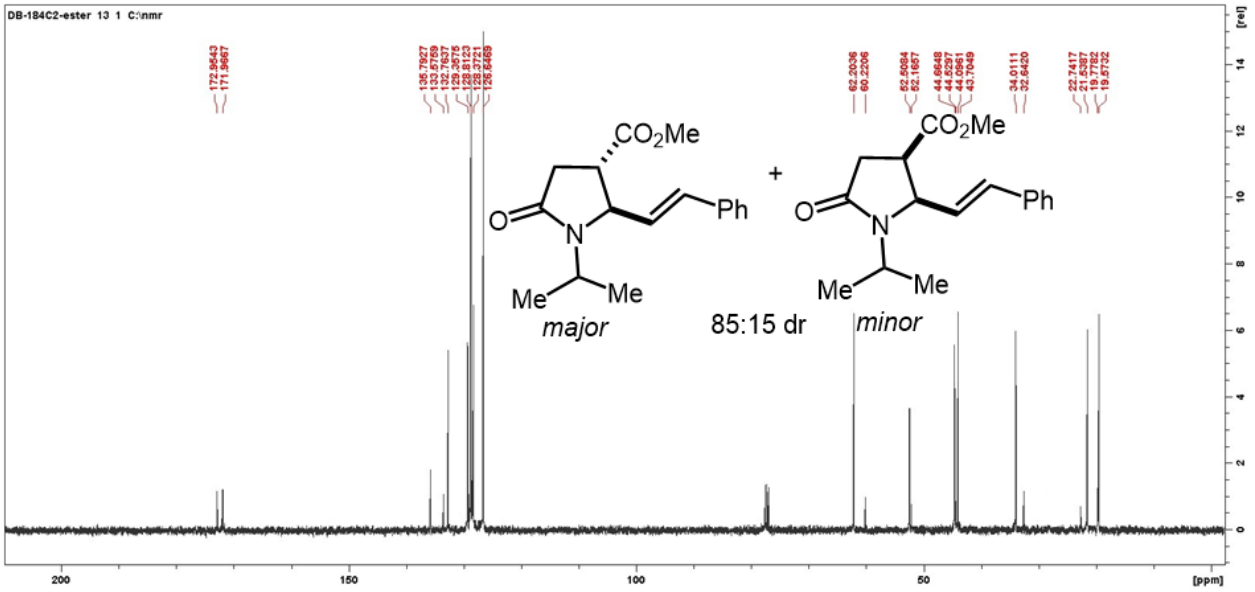
Ph
Me
Me
major
+
85:15 dr
minor
[ppm]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+
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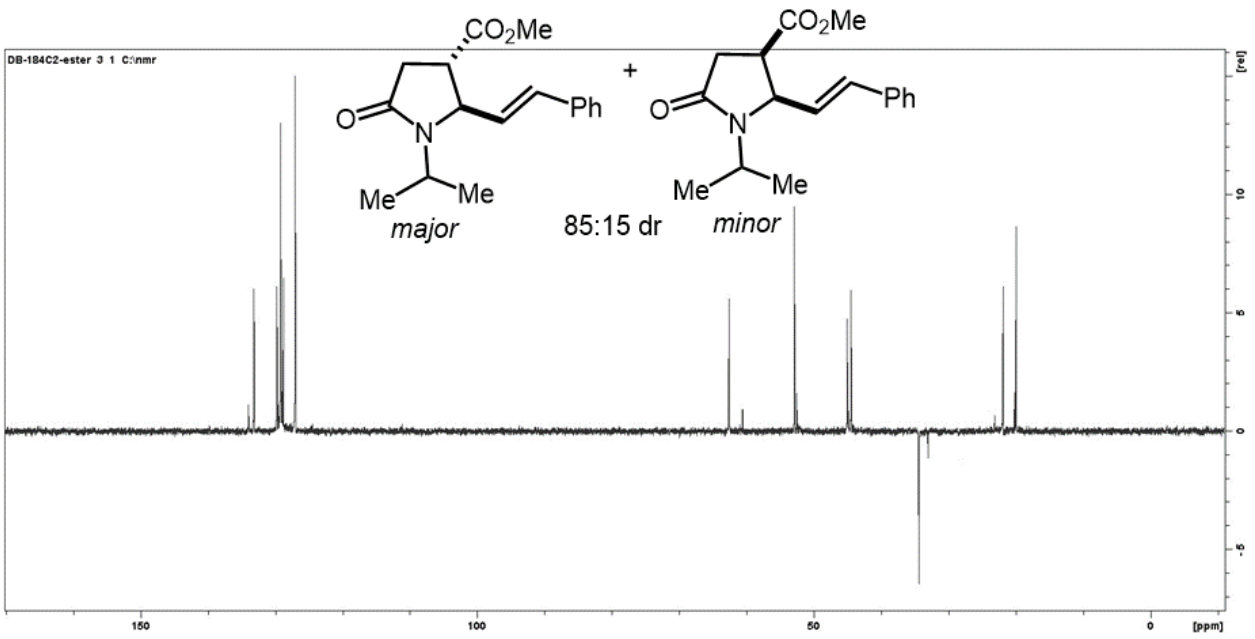
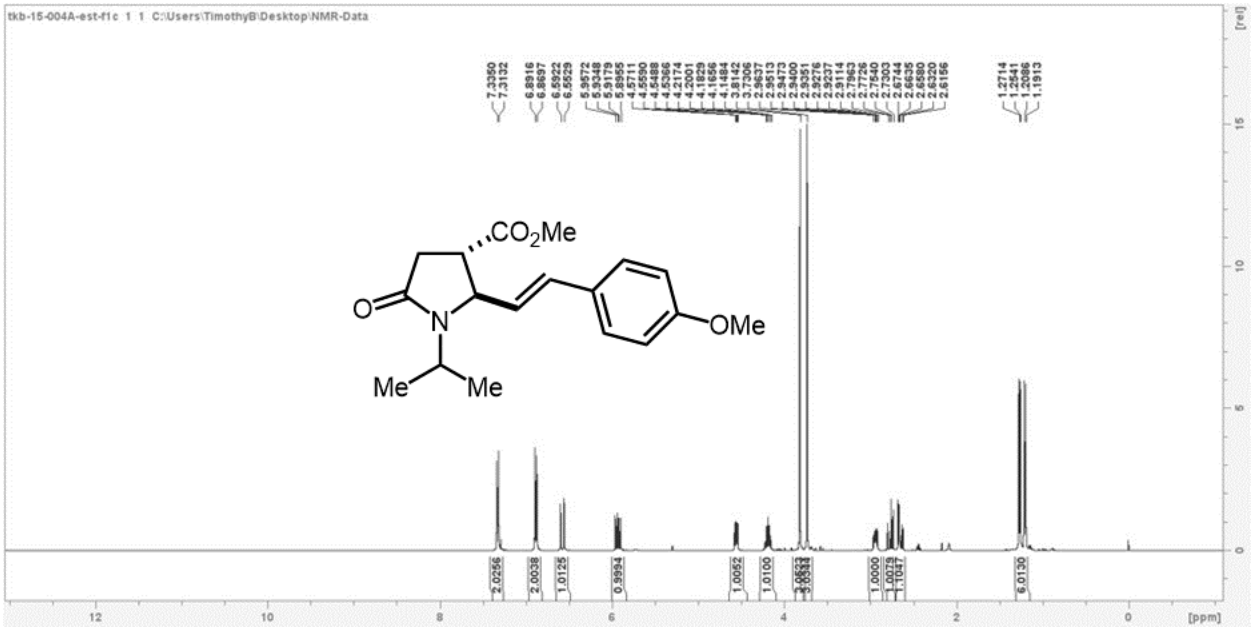
[ppm]



Compound 3i

Prepared in 1.0 mmol scale using **General Procedure A**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 50:50). Yellowish oil. Yield = 253.9 mg, 80%, 95:5 dr (*anti:syn*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, *J* = 8.7 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 6.57 (d, *J* = 15.7 Hz, 1H), 5.93 (dd, *J* = 15.7, 9.0 Hz, 1H), 4.55 (dd, *J* = 8.9, 4.9 Hz, 1H), 4.18 (hept, *J* = 6.9 Hz, 1H), 3.81 (s, 3H), 3.73 (s, 3H), 2.94 (ddd, *J* = 9.5, 6.6, 4.9 Hz, 1H), 2.76 (dd, *J* = 16.9, 9.5 Hz, 1H), 2.65 (dd, *J* = 17.0, 6.6 Hz, 1H), 1.26 (d, *J* = 7.0 Hz, 3H), 1.17 (dd, *J* = 22.9, 6.7 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.99, 171.89, 159.78, 132.24, 128.51, 127.84, 127.01, 114.17, 62.39, 55.33, 52.40, 44.63, 44.25, 34.02, 21.42, 19.52. **HRMS-EI$^+$** (*m/z*): calc for $C_{18}H_{23}NO_4$ $[M]^+$ 317.1627, found 317.1622.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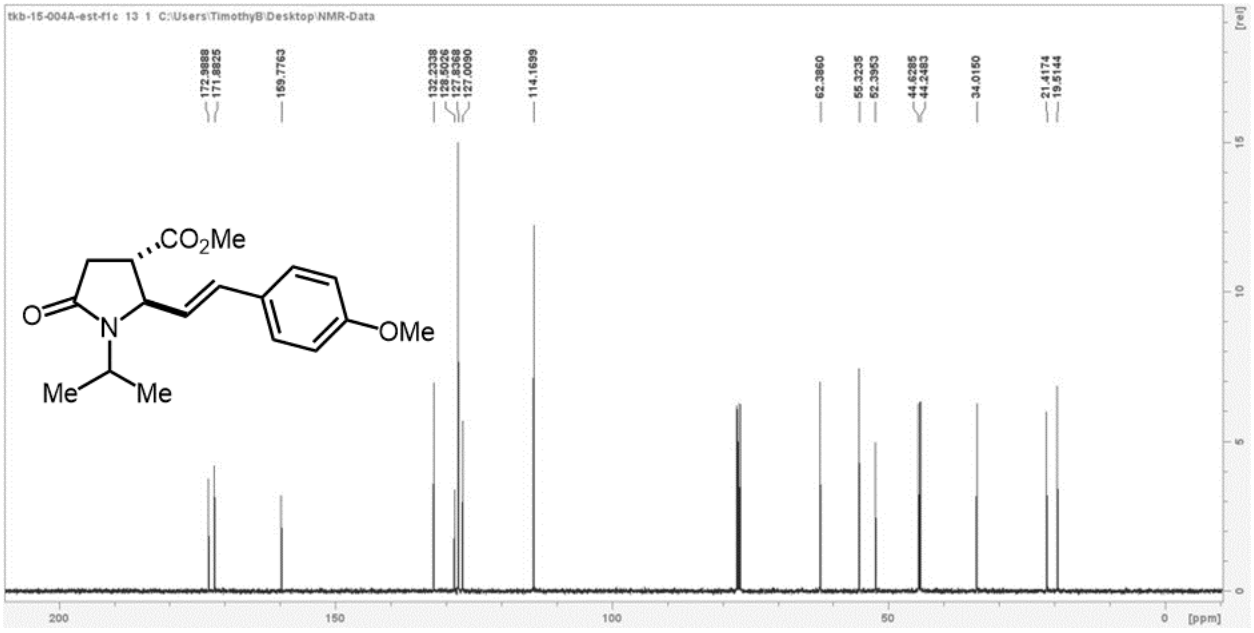
CO2Me
O
N
OMe
Me
Me
[ppm]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CO2Me
O
N
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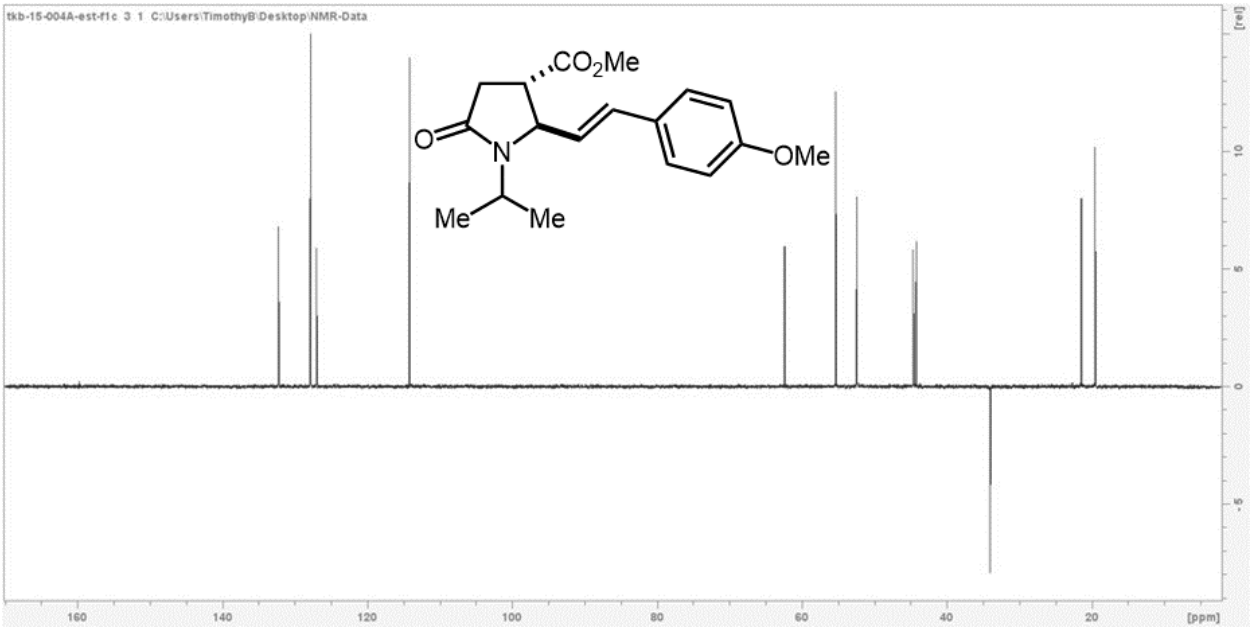
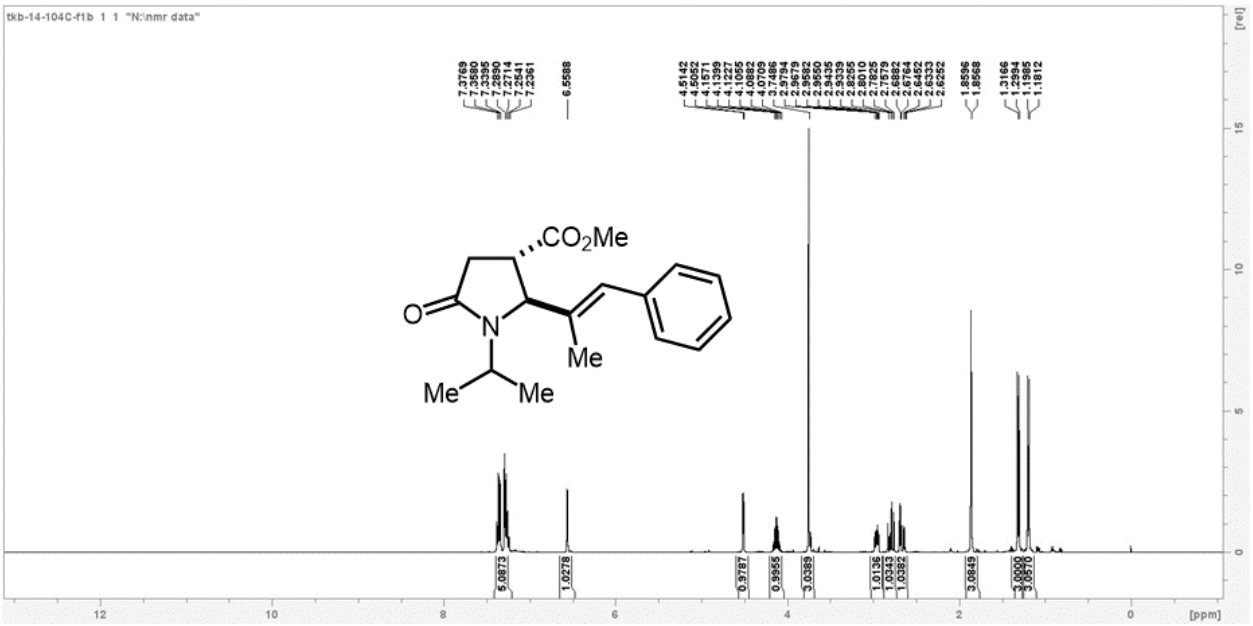
Me
Me
[ppm]



Compound 3j

Prepared in 1.0 mmol scale using **General Procedure A**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 70:30). Yellowish oil. Yield = 265.2 mg, 88%, 95:5 dr (*anti:syn*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.32 (m, 2H), 7.32 – 7.21 (m, 3H), 6.56 (s, 1H), 4.51 (d, J = 3.6 Hz, 1H), 4.12 (hept, J = 6.9 Hz, 1H), 3.75 (s, 3H), 2.96 (ddd, J = 9.9, 4.7, 3.6 Hz, 1H), 2.79 (dd, J = 17.2, 9.8 Hz, 1H), 2.66 (dd, J = 17.2, 4.7 Hz, 1H), 1.86 (d, J = 1.4 Hz, 3H), 1.31 (d, J = 6.9 Hz, 3H), 1.19 (d, J = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.44, 172.81, 136.65, 136.51, 128.89, 128.80, 128.32, 127.09, 67.39, 52.47, 45.09, 42.04, 34.21, 20.05, 19.52, 13.38. FTIR (KBr): 2984.1, 1723.4, 1669.4, 1608.2, 1511.1, 1431.8, 1414.7, 1344.9, 1298.4, 1135.3, 1031.8, 996.7, 702.4. **HRMS-EI^{+}** (*m/z*): calc for $C_{18}H_{23}NO_3$ $[M]^{+}$ 301.1678, found 301.1684.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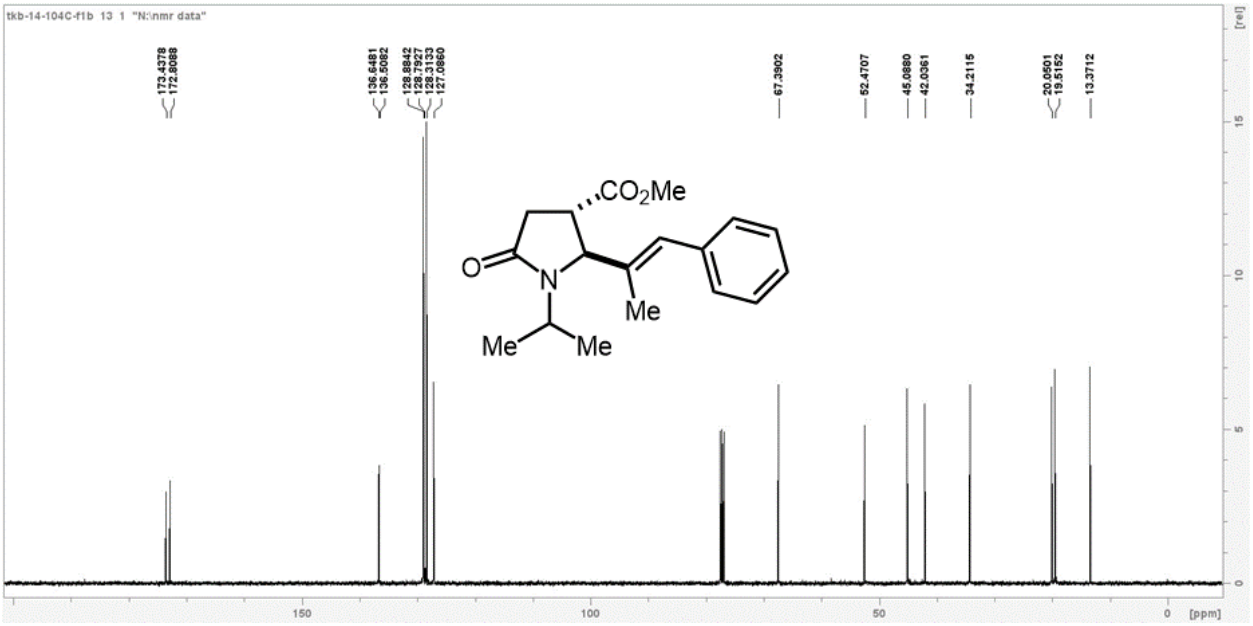
CO2Me
O
N
Me
Me
Me
[rel]
[ppm]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O
N
Me
Me
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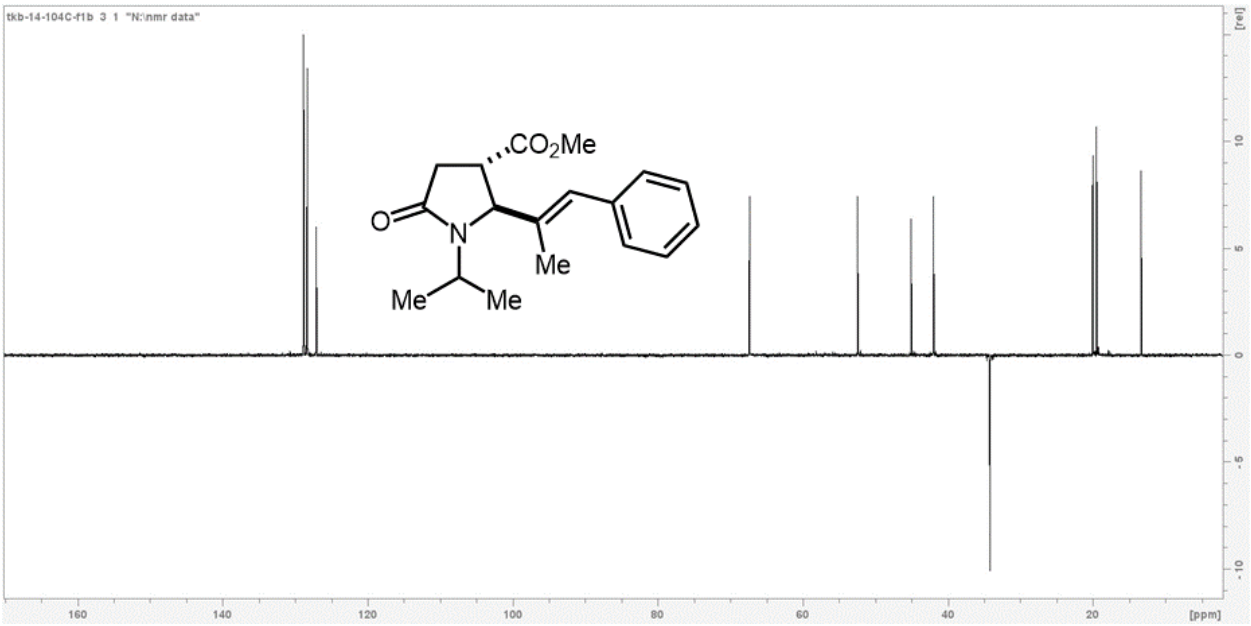
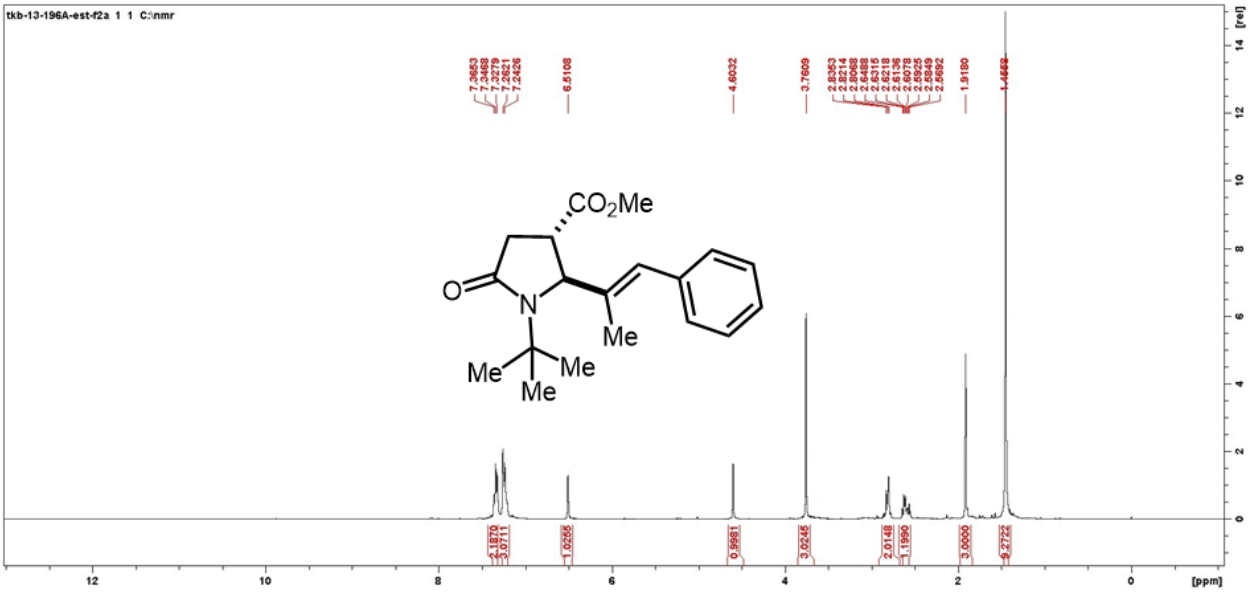
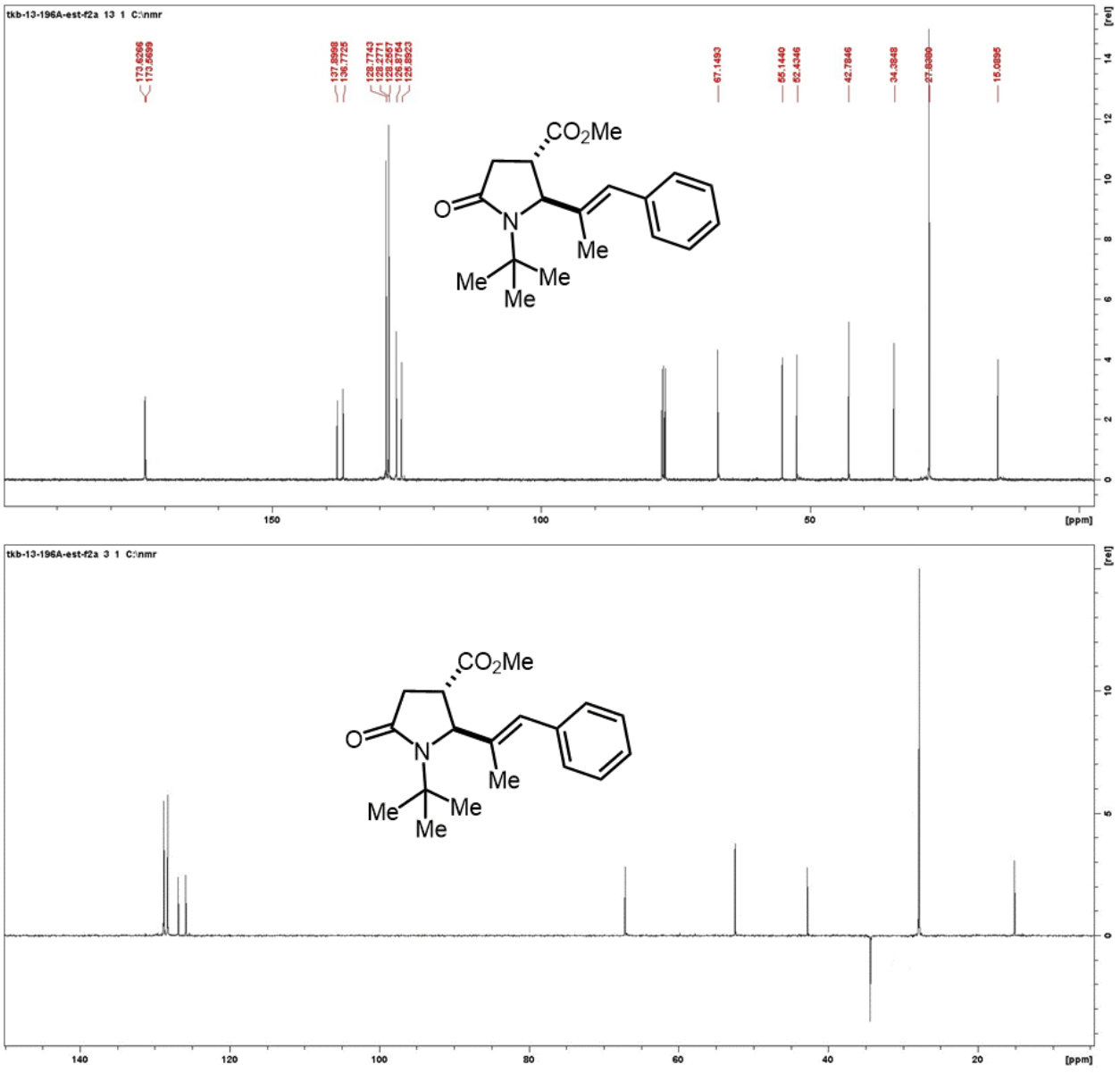


Compound 3k

Prepared in 1.0 mmol scale using **General Procedure A**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 70:30). Yellowish oil. Yield = 271.2 mg, 86%, 95:5 dr (*anti:syn*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (dd, *J* = 9.9, 5.2 Hz, 2H), 7.24 (dd, *J* = 12.3, 9.3 Hz, 3H), 6.51 (s, 1H), 4.60 (s, 1H), 3.76 (s, 3H), 2.89 – 2.76 (m, 2H), 2.67 – 2.52 (m, 1H), 1.92 (d, *J* = 1.5 Hz, 3H), 1.46 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.63, 173.57, 137.90, 136.78, 128.84, 128.78, 128.28, 128.26, 126.88, 125.90, 67.15, 55.15, 52.44, 42.79, 34.39, 27.84, 15.09. **HRMS-EI^{+}** (*m/z*): calc for $C_{19}H_{25}NO_3$ $[M]^{+}$ 315.1834, found 315.1830.

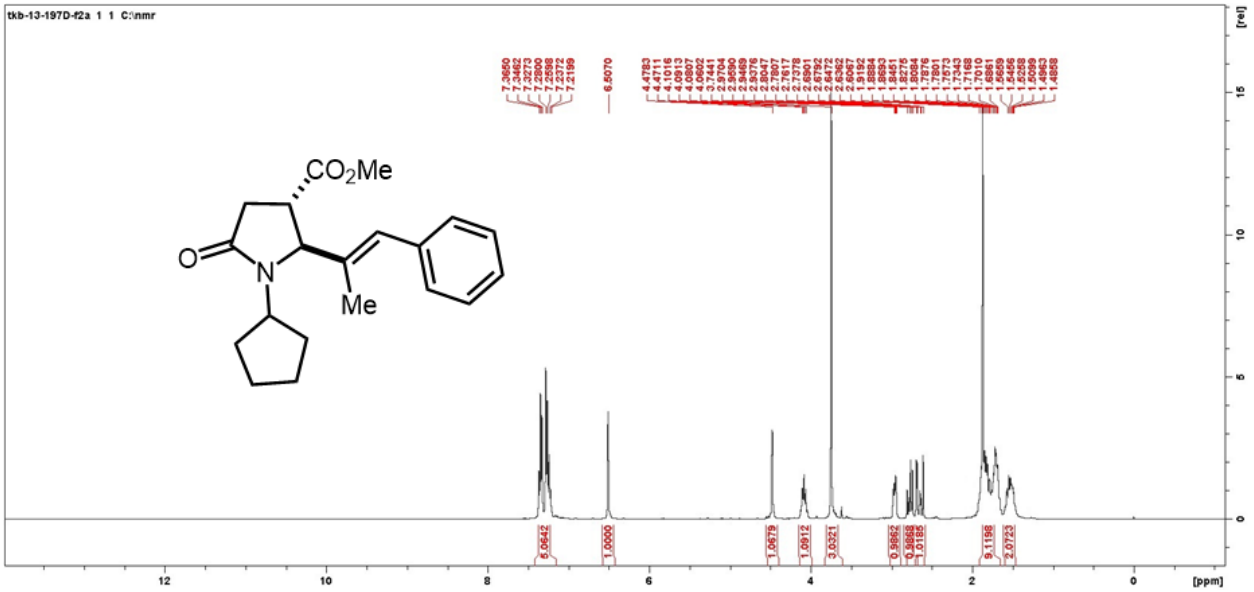


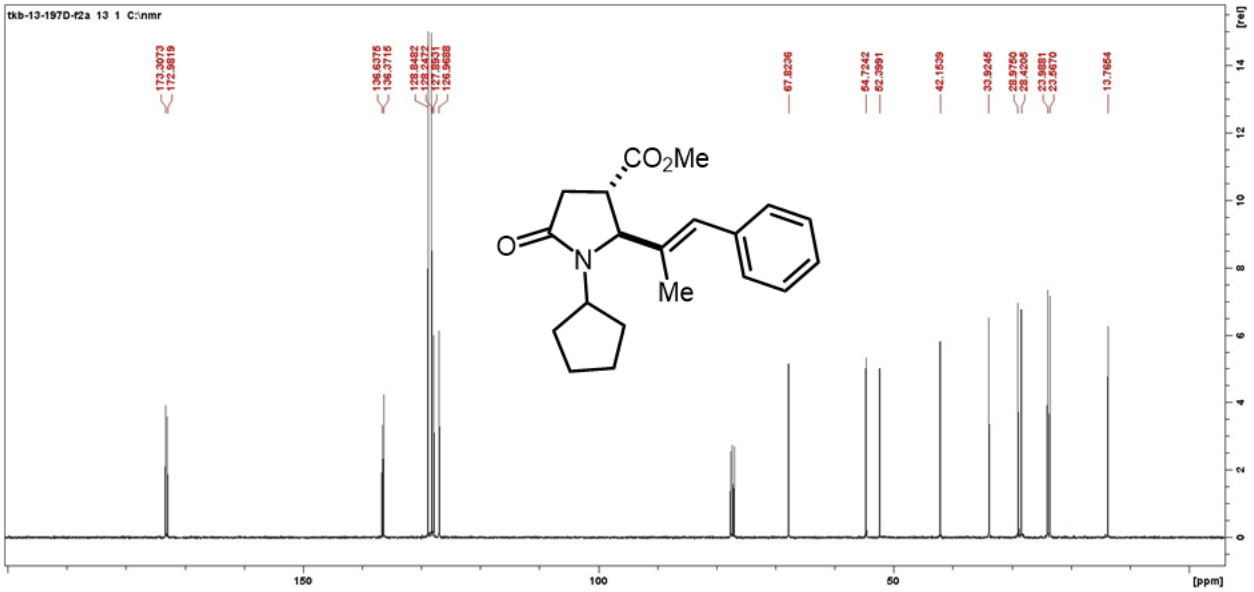


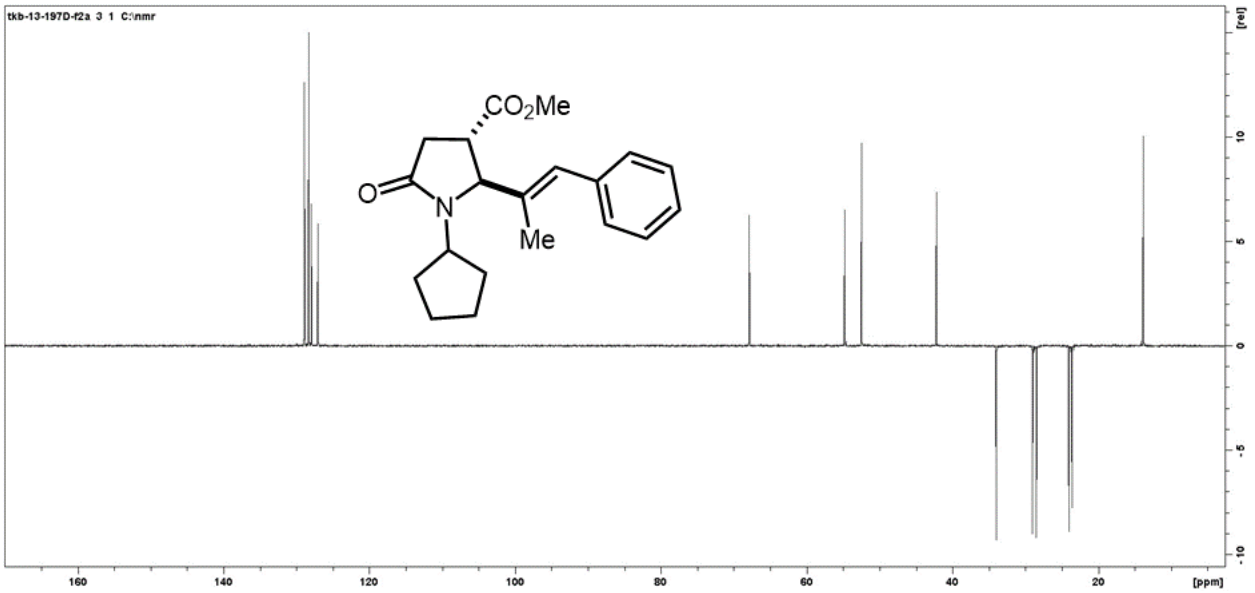
Compound 3l

Prepared in 1.0 mmol scale using **General Procedure A**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 70:30). Yellowish oil. Yield = 278.3 mg, 85%, 95:5 dr (*anti*:*syn*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (d, *J* = 7.5 Hz, 2H), 7.25 (dd, *J* = 16.7, 7.6 Hz, 3H), 6.51 (s, 1H), 4.47 (d, *J* = 3.3 Hz, 1H), 4.15 – 4.02 (m, 1H), 3.74 (s, 3H), 2.77 (dd, *J* = 17.2, 9.6 Hz, 1H), 2.71 – 2.58 (m, 2H), 1.81 – 1.69 (m, 9H), 1.62 – 1.43 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.31, 172.99, 136.64, 136.37, 128.85, 128.25, 127.90, 126.97, 67.83, 54.73, 52.40, 42.16, 33.93, 28.98, 28.42, 23.99, 23.57, 13.77. FTIR (KBr): 2965.4, 1727.5, 1696.3, 1604.9,

1511.0, 1448.5, 1414.7, 1384.9, 1357.4, 1298.7, 1247.5, 1179.3, 1135.9, 1031.8, 905.8, 839.0. **HRMS-EI**$^{+}$ (*m/z*): calc for $C_{20}H_{25}NO_3$ $[M]^{+}$ 327.1834, found 327.1838.

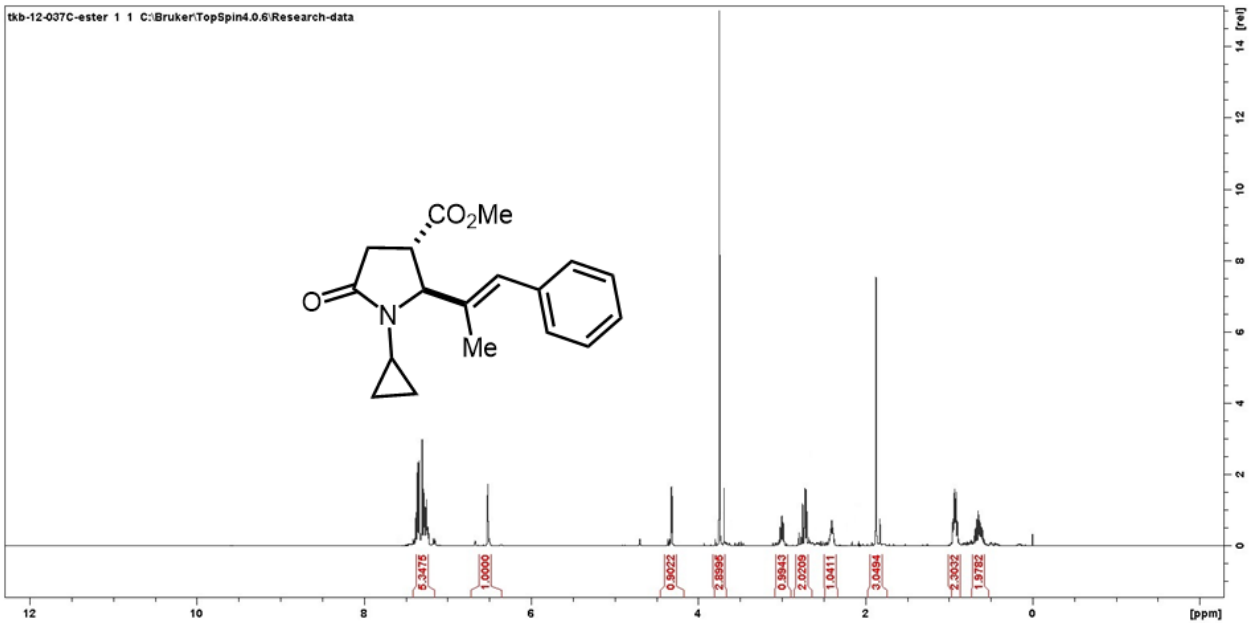






Compound 3m

Prepared in 1.0 mmol scale using **General Procedure A**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 70:30). Yellowish oil. Yield = 242.5 mg, 81%, 90:10 dr (*anti:syn*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 – 7.00 (m, 5H), 6.31 (d, J = 1.6 Hz, 1H), 4.19 – 4.09 (m, 1H), 3.54 (s, 3H), 2.90 – 2.75 (m, 1H), 2.62 – 2.52 (m, 1H), 2.55 – 2.48 (m, 2H), 2.21 – 2.14 (m, 1H), 1.69 (s, 3H), 0.80 – 0.64 (m, 2H), 0.58 – 0.33 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.84, 173.40, 136.70, 135.00, 129.02, 128.80, 128.35, 127.13, 69.56, 52.61, 41.42, 34.18, 24.28, 13.61, 6.74, 4.88. FTIR (KBr): 2984.1, 1733.5, 1654.3, 1606.9, 1511.0, 1448.5, 1414.7, 1384.9, 1357.4, 1299.7, 1242.5, 1179.3, 1031.8, 994.9, 823.7, 735.2. **HRMS-EI$^+$** (*m/z*): calc for $C_{18}H_{21}NO_3$ $[M]^+$ 299.1521, found 299.1527.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O
N
Me
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1.0000
0.9022
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0.9943
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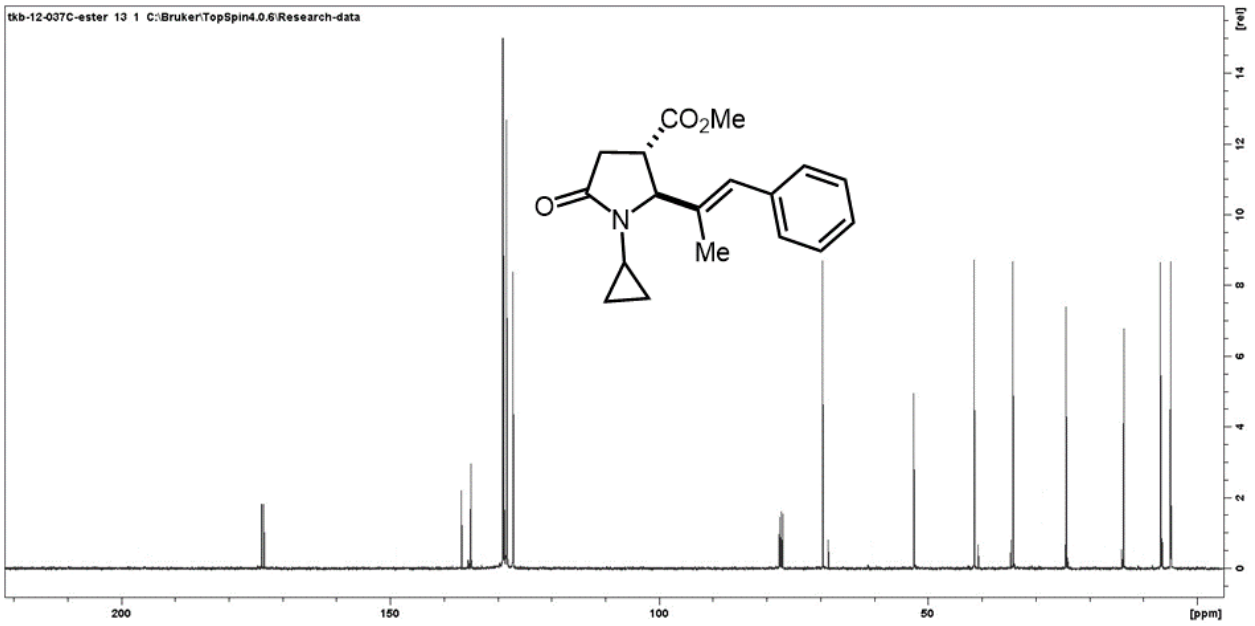
2.3032
1.9782
12
10
8
6
4
2
0
[ppm]
[rel]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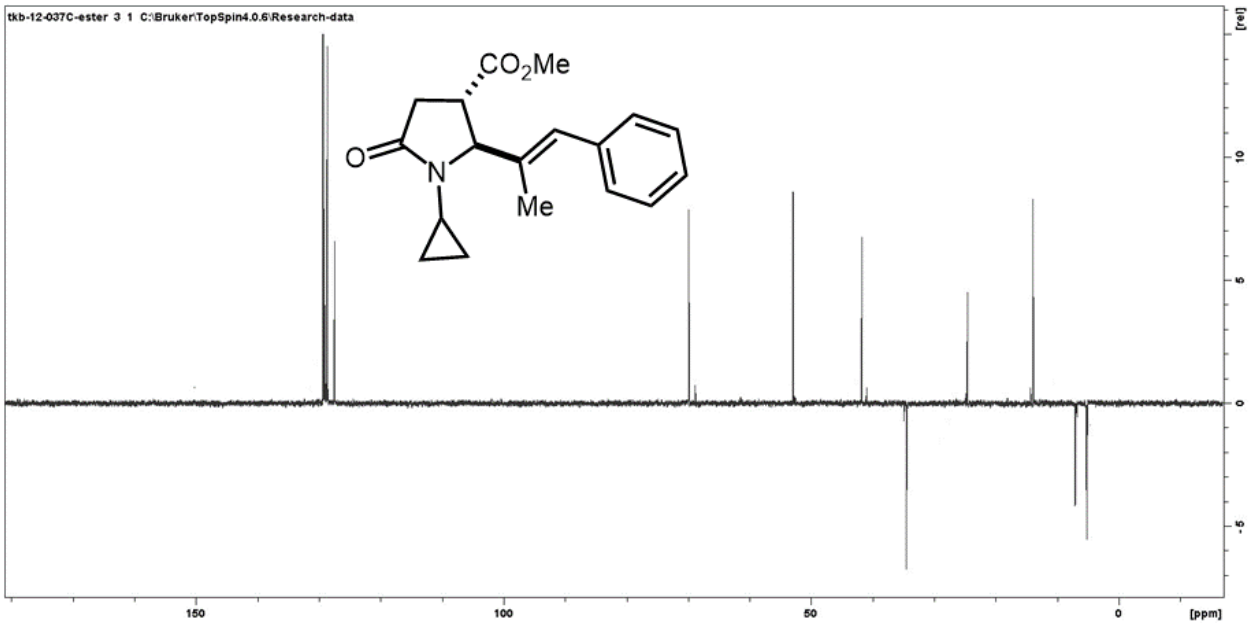
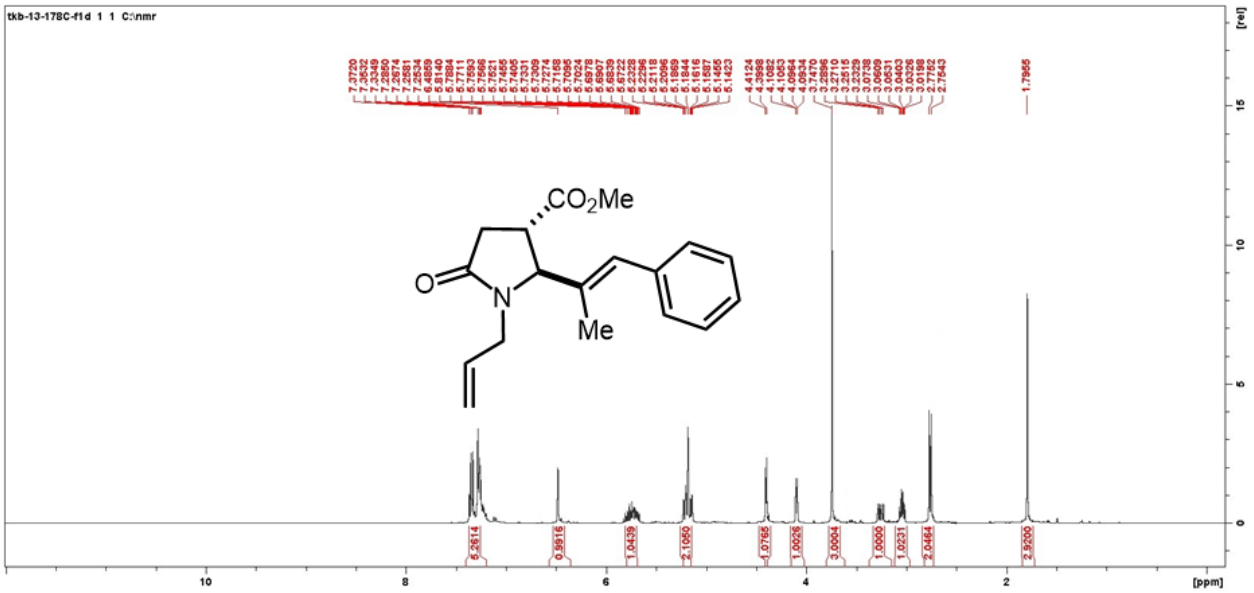
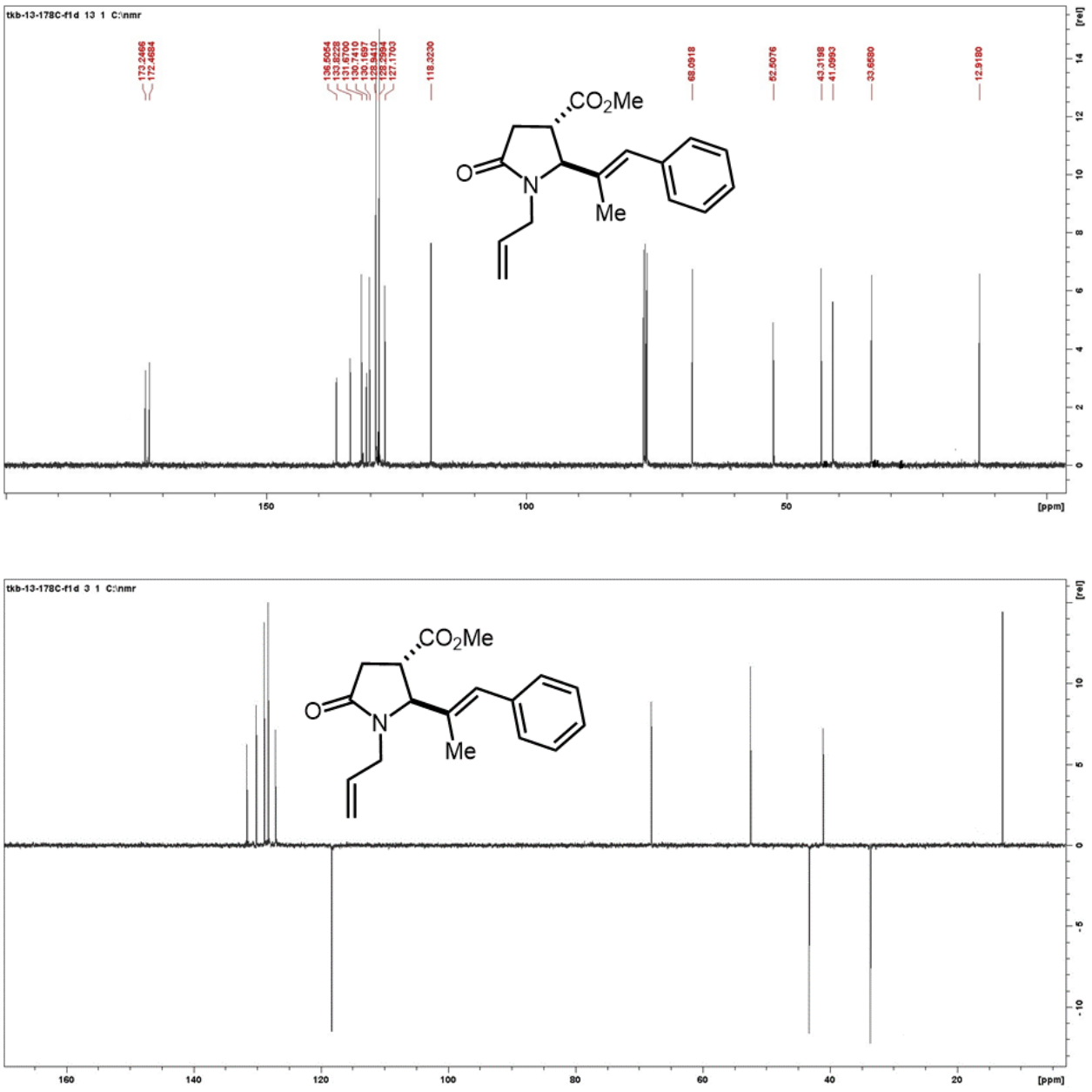


Compound 3n

Prepared in 1.0 mmol scale using **General Procedure A**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 80:20). Yellowish oil. Yield = 257.5 mg, 86%, 95:5 dr (*trans:cis*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.17 (m, 5H), 6.49 (d, *J* = 1.4 Hz, 1H), 5.85 – 5.65 (m, 1H), 5.26 – 5.12 (m, 2H), 4.50 – 4.33 (m, 1H), 4.10 (dt, *J* = 6.0, 1.4 Hz, 1H), 3.75 (s, 3H), 3.26 (dd, *J* = 15.2, 7.4 Hz, 1H), 3.05 (td, *J* = 8.3, 5.1 Hz, 1H), 2.76 (d, *J* = 8.3 Hz, 2H), 1.79 (d, *J* = 1.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.25, 172.47, 136.51, 133.83, 131.67, 130.75, 130.17, 128.94, 128.30, 127.17, 118.33, 68.10, 52.51, 43.32, 41.10, 33.66, 28.19, 12.92. **HRMS-EI^{+}** (*m/z*): calc for $C_{18}H_{21}NO_3$ $[M]^{+}$ 299.1521, found 299.1527.

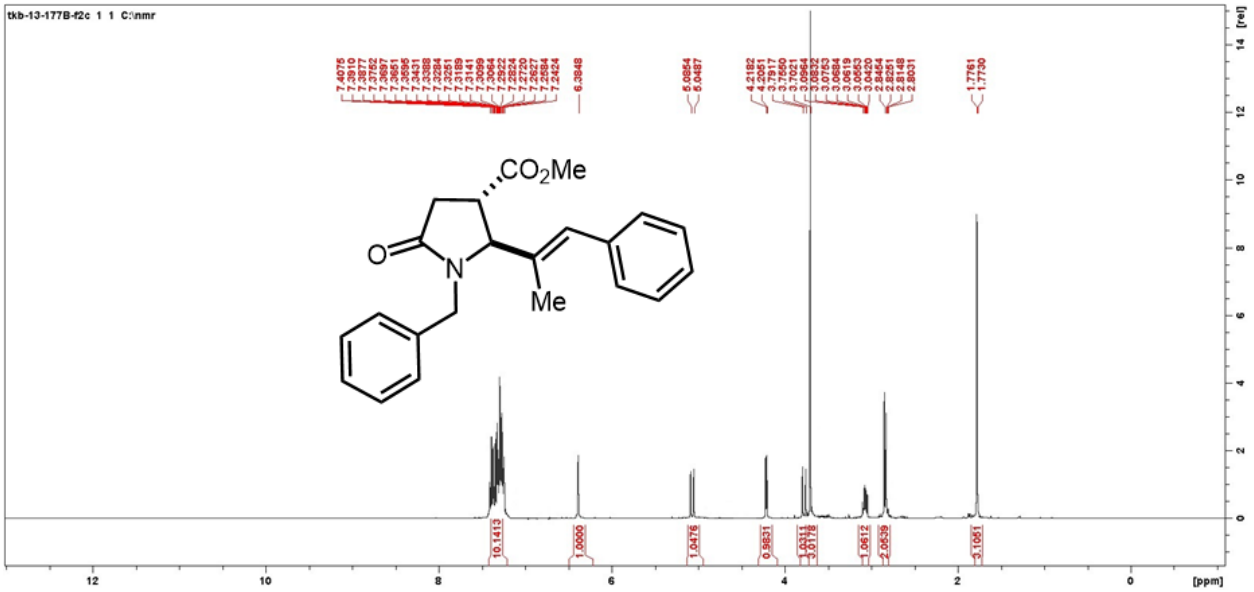


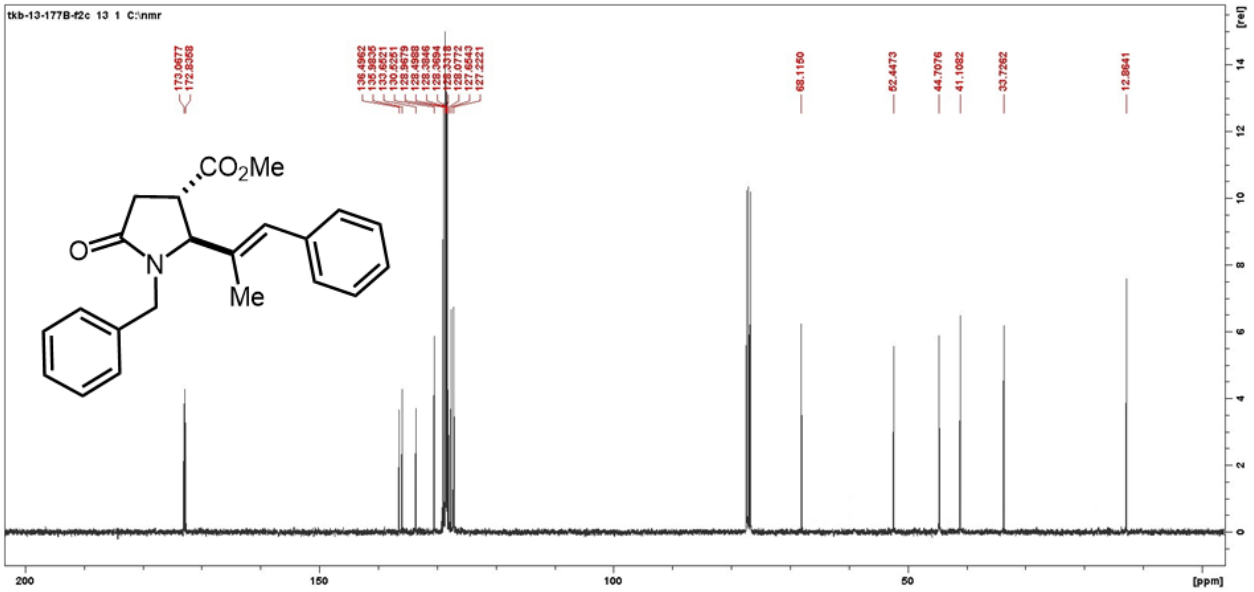


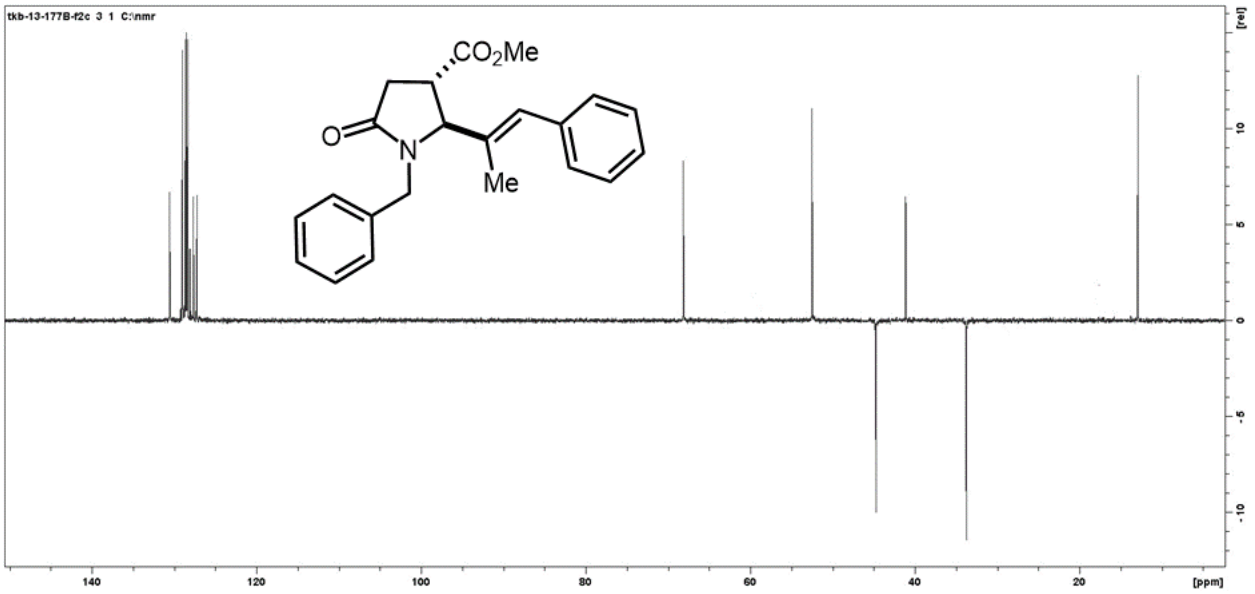
Compound 3o

Prepared in 1.0 mmol scale using **General Procedure A**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 50:50). Greenish-yellow oil. Yield = 293.5 mg, 84%, 95:5 dr (*trans:cis*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.24 (m, 10H), 6.38 (d, J = 1.4 Hz, 1H), 5.06 (d, J = 14.7 Hz, 1H), 4.21 (d, J = 5.2 Hz, 1H), 3.78 (d, J = 14.7 Hz, 1H), 3.70 (s, 3H), 3.13 – 3.02 (m, 1H), 2.93 – 2.76 (m, 2H), 1.77 (d, J = 1.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.07, 172.84, 136.50, 135.99, 133.66, 130.53, 128.97, 128.61, 128.50, 128.39, 128.37, 128.33, 128.08,

127.66, 127.23, 68.12, 52.45, 44.71, 41.11, 33.73, 12.87. **HRMS-EI**$^{+}$ (*m/z*): calc for $C_{22}H_{23}NO_3$ $[M]^{+}$ 349.1678, found 349.1674.

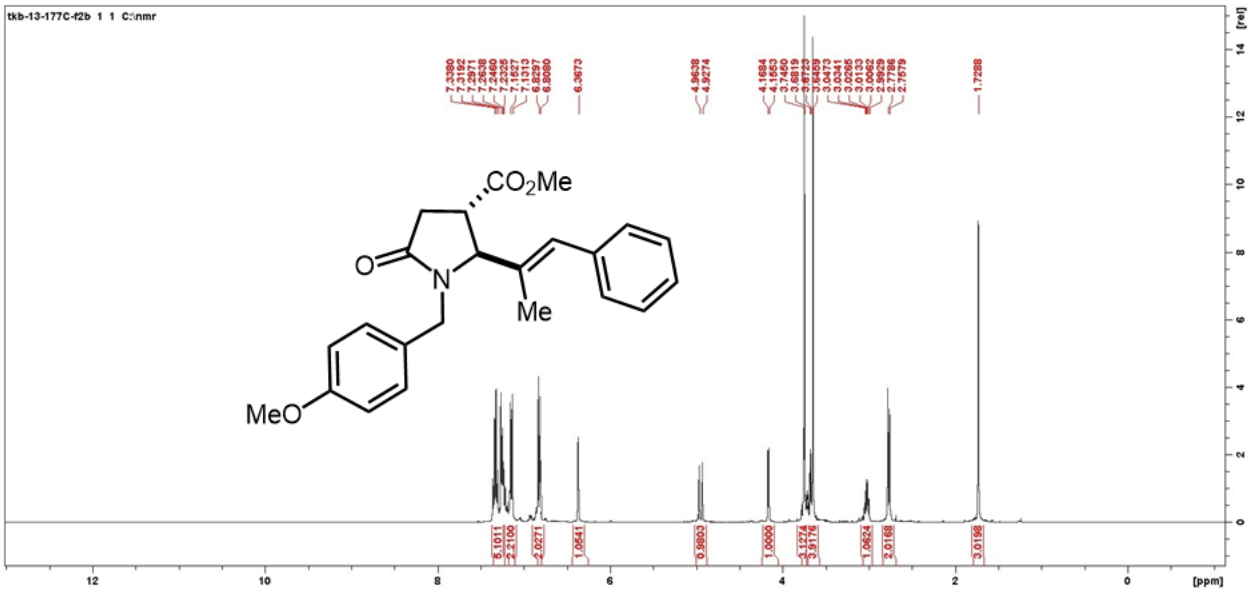


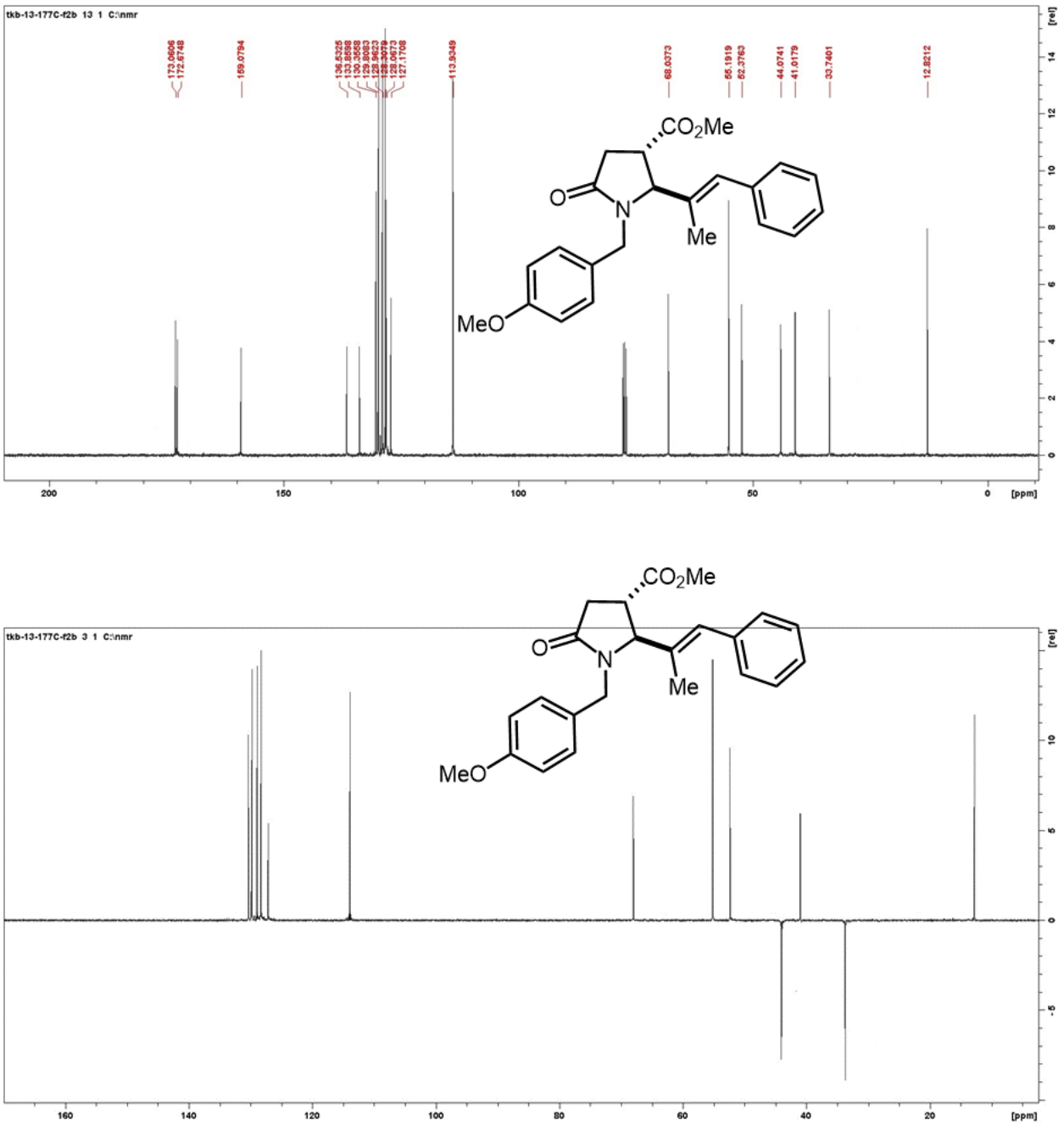




Compound 3p

Prepared in 1.0 mmol scale using **General Procedure A**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 30:70). Greenish-yellow oil. Yield = 333.9 mg, 88%, 95:5 dr (*trans:cis*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.13 (m, 7H), 6.81 (d, *J* = 7.9 Hz, 2H), 6.37 (d, *J* = 1.9 Hz, 1H), 4.92 (d, *J* = 14.9 Hz, 1H), 4.16 (d, *J* = 5.3 Hz, 1H), 3.75 (s, 3H), 3.71 (d, *J* = 2.3 Hz, 1H), 3.65 (s, 3H), 3.04 – 2.97 (m, 1H), 2.77 (d, *J* = 8.3 Hz, 2H), 1.73 (d, *J* = 1.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.06, 172.68, 159.08, 136.54, 133.86, 130.36, 129.81, 128.97, 128.31, 128.07, 127.18, 113.94, 113.90, 68.04, 55.20, 52.38, 44.08, 41.02, 33.74, 12.82. **HRMS-EI$^+$** (*m/z*): calc for $C_{23}H_{25}NO_4$ $[M]^+$ 379.1784, found 379.1789.

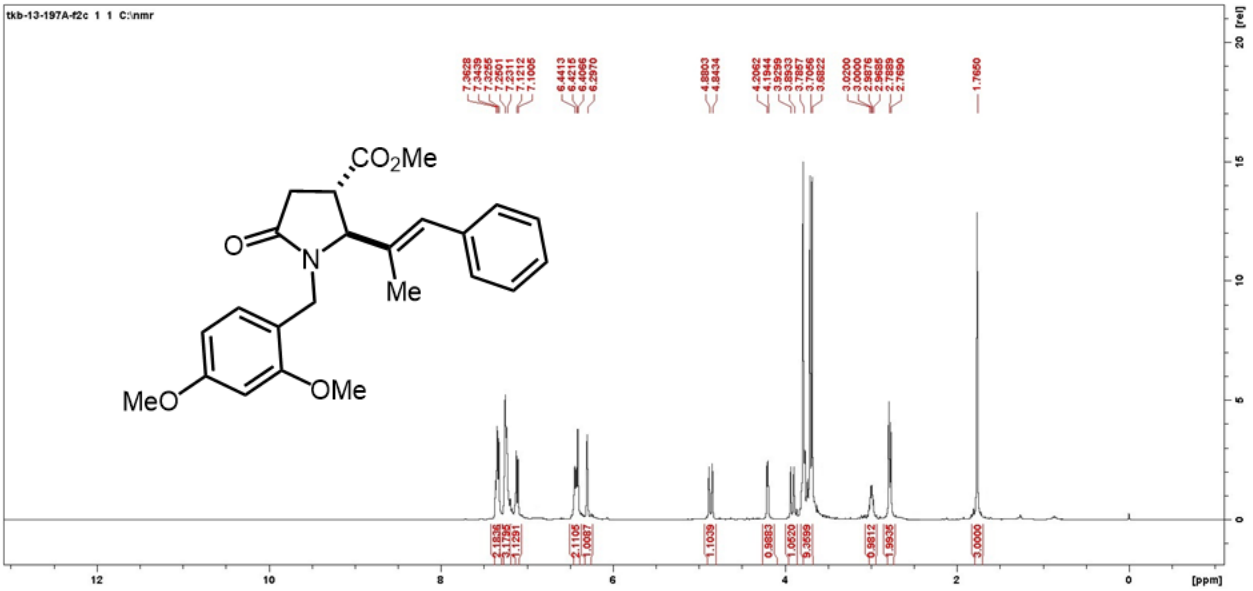


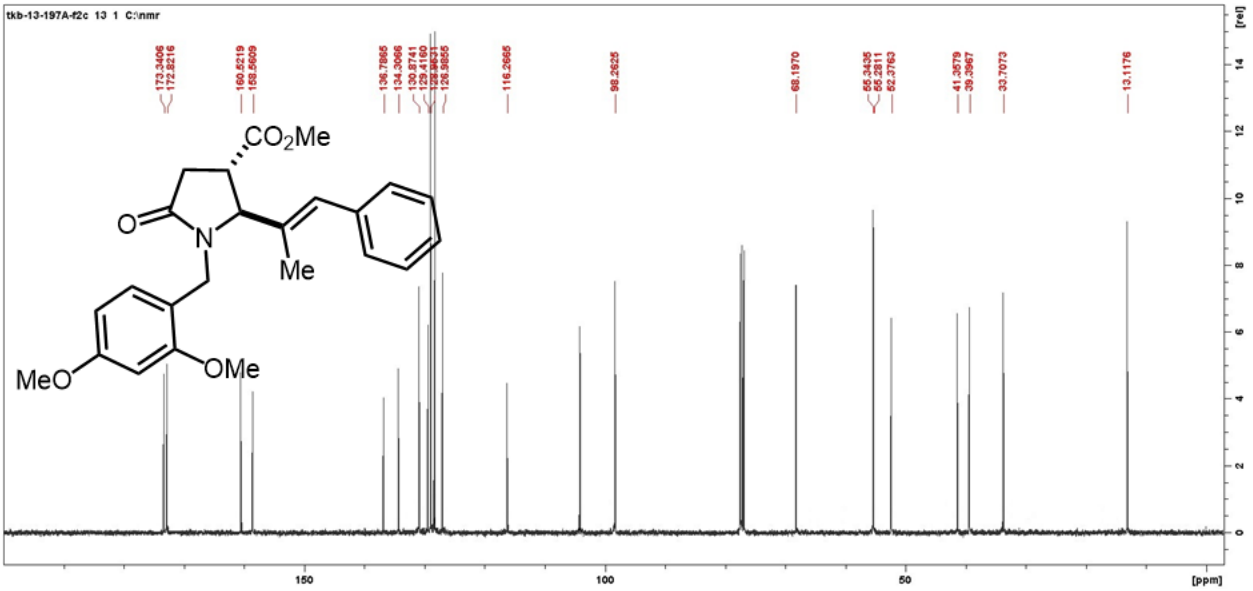


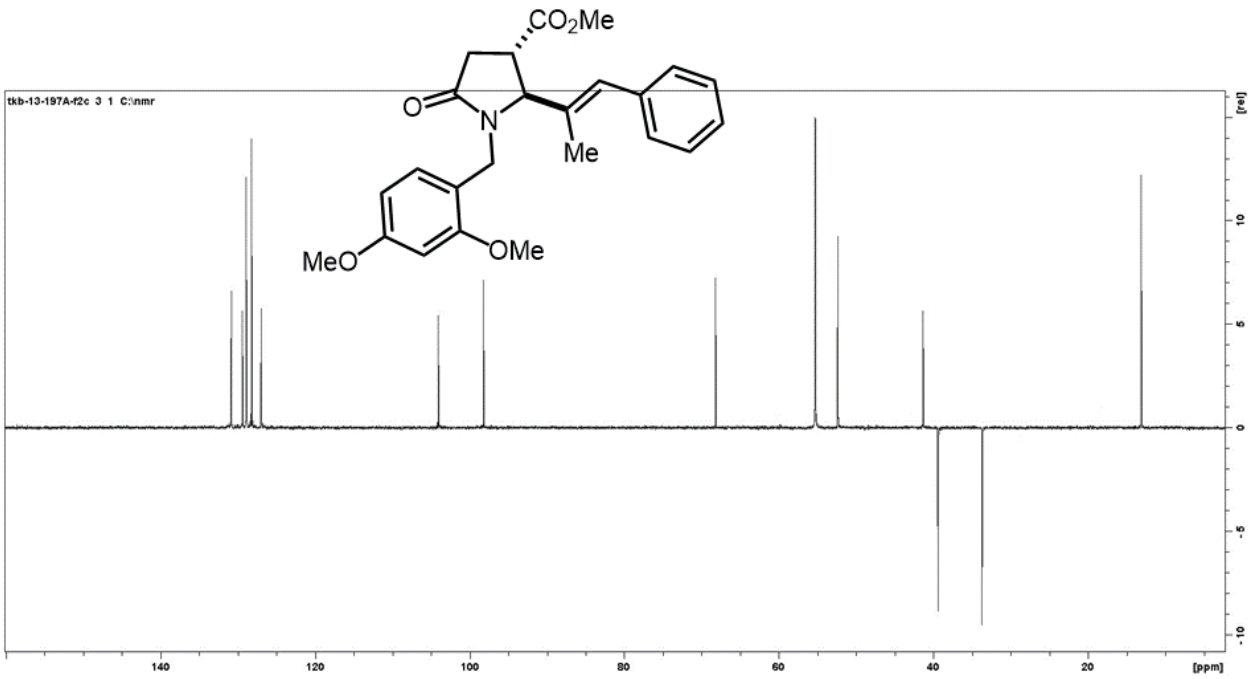
Compound 3q

Prepared in 1.0 mmol scale using **General Procedure A**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 30:70). Greenish-yellow oil. Yield = 344.0 mg, 84%, 95:5 dr (*trans:cis*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (t, J = 7.6 Hz, 2H), 7.26 – 7.08 (m, 4H), 6.48 – 6.33 (m, 2H), 6.30 (s, 1H), 4.86 (d, J = 14.7 Hz, 1H), 4.20 (d, J = 4.8 Hz, 1H), 3.91 (d, J = 14.7 Hz, 1H), 3.84 – 3.63 (m, 9H), 2.99 (td, J = 8.0, 4.7 Hz, 1H), 2.78 (d, J = 8.0 Hz, 2H), 1.77 (s,

3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.34, 172.83, 160.53, 158.57, 136.79, 134.31, 130.88, 129.42, 128.96, 128.26, 128.23, 126.99, 116.27, 104.11, 98.27, 68.20, 55.35, 55.29, 52.38, 41.36, 39.40, 33.71, 13.12. **HRMS-EI$^+$** (*m/z*): calc for $C_{24}H_{27}NO_5$ $[M]^+$ 409.1889, found 409.1886.

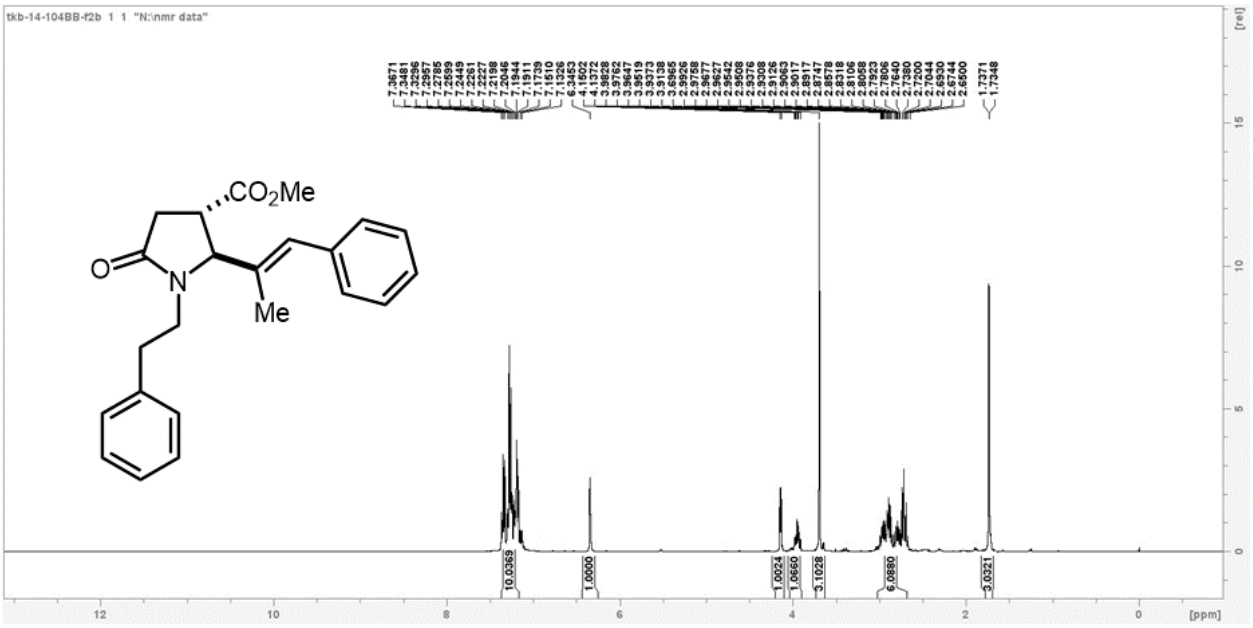






Compound 3r

Prepared in 1.0 mmol scale using **General Procedure A**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 70:30). Pale-yellow oil. Yield = 308.9 mg, 85%, 95:5 dr (*trans:cis*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.08 (m, 10H), 6.35 (s, 1H), 4.14 (d, J = 5.2 Hz, 1H), 4.02 – 3.89 (m, 1H), 3.70 (s, 3H), 3.04 – 2.63 (m, 6H), 1.73 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.01, 172.68, 138.85, 136.51, 134.04, 130.28, 129.00, 128.90, 128.61, 128.58, 128.35, 127.23, 126.52, 69.09, 52.45, 42.34, 41.18, 33.58, 12.79. **HRMS-EI$^+$** (*m/z*): calc for $C_{23}H_{25}NO_3$ $[M]^+$ 363.1834, found 363.1839.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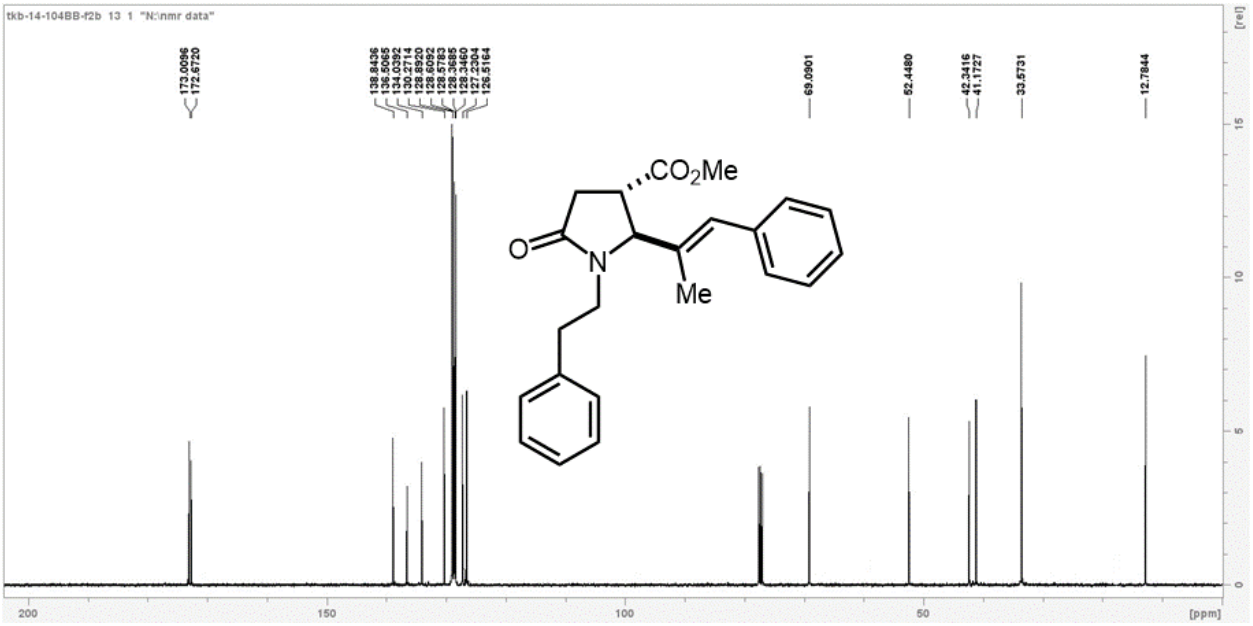
CO2Me
O
N
Me
[ppm]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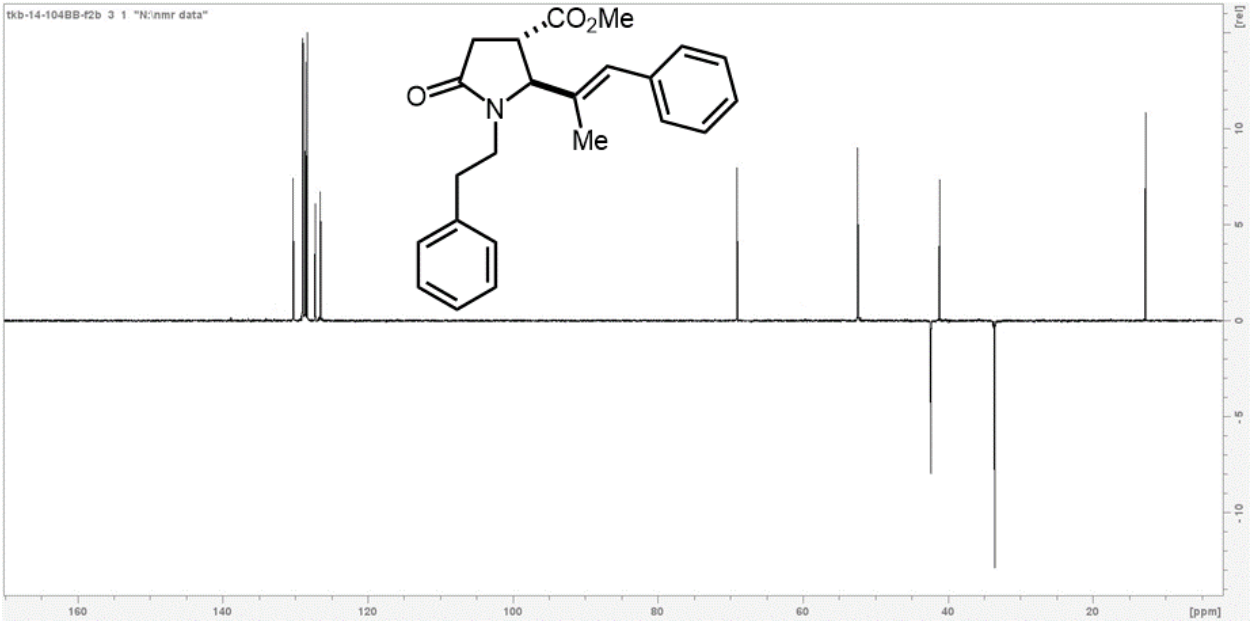
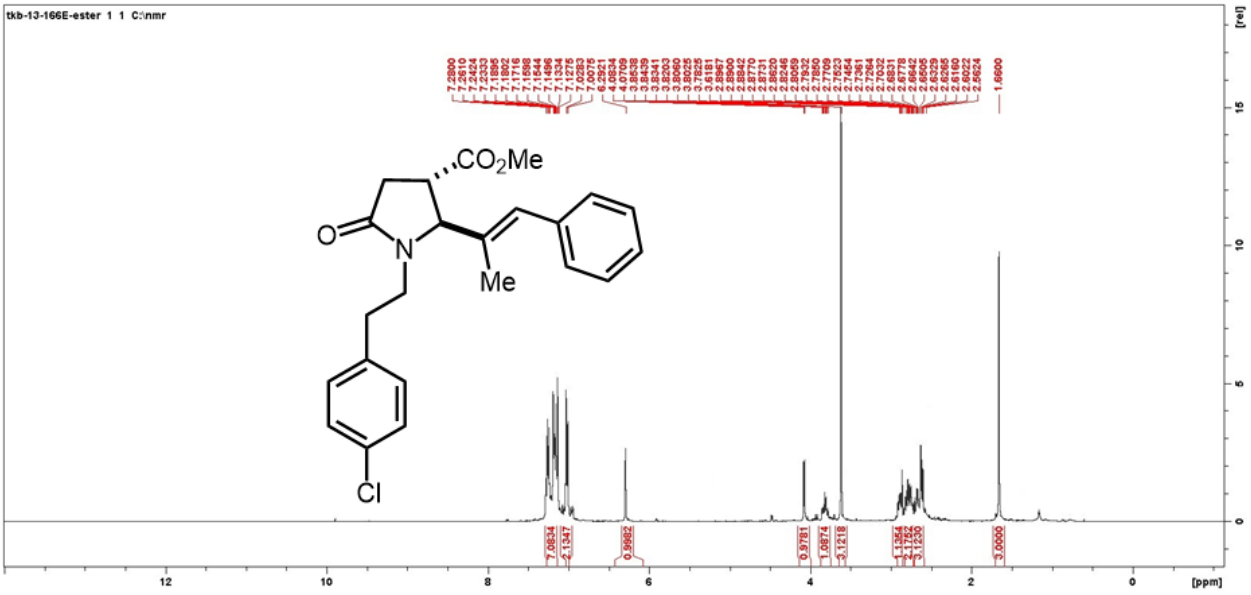
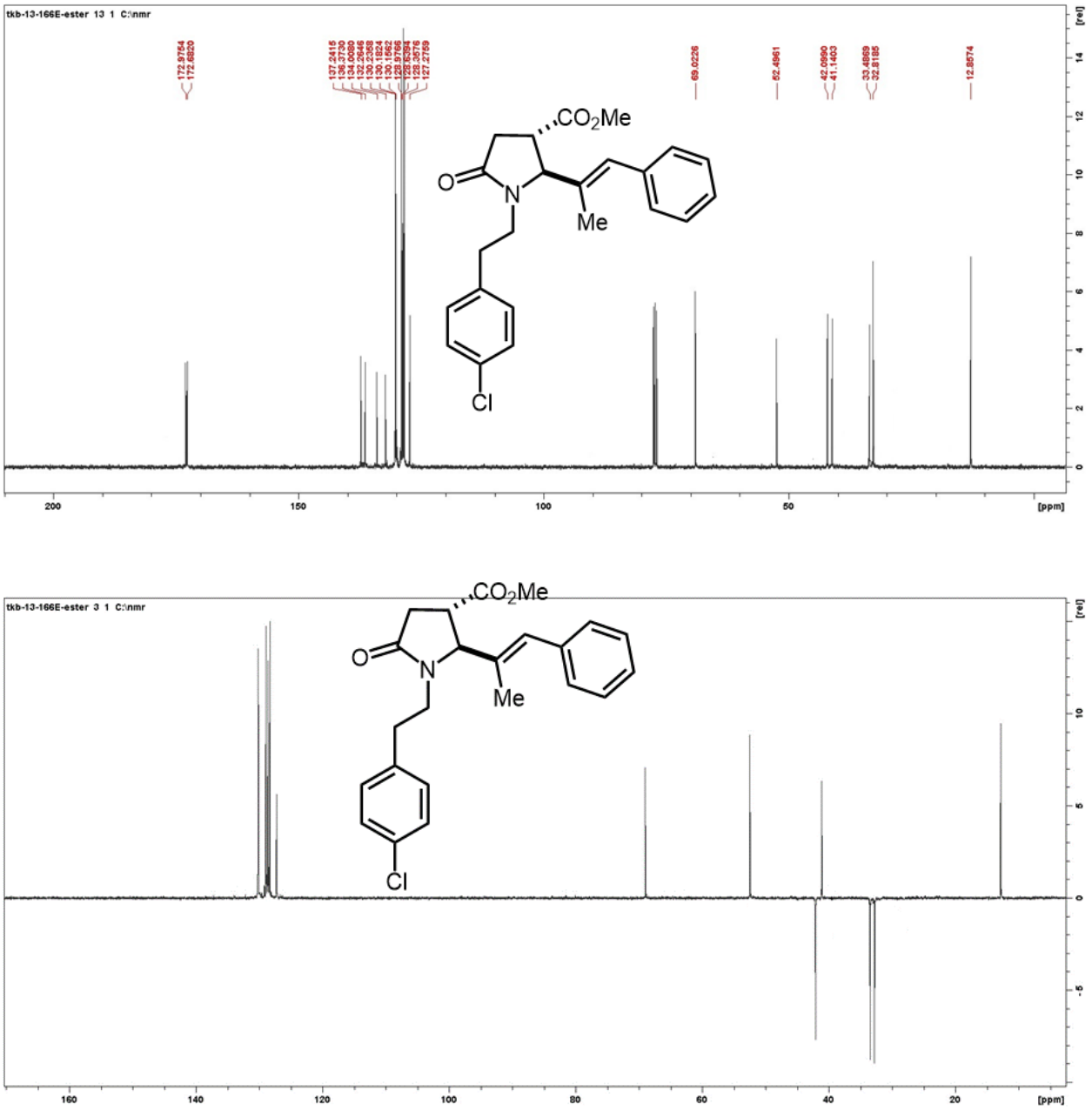
O
N
Me
[ppm]



Compound 3s

Prepared in 1.0 mmol scale using **General Procedure A**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 70:30). Pale-yellow oil. Yield = 326.3 mg, 82%, 95:5 dr (*trans:cis*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.10 (m, 9H), 6.29 (s, 1H), 4.08 (d, J = 5.0 Hz, 1H), 3.82 (ddd, J = 15.1, 8.8, 5.8 Hz, 1H), 3.62 (s, 3H), 2.96 – 2.50 (m, 6H), 1.66 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.98, 172.68, 137.25, 136.38, 134.01, 132.27, 130.24, 130.19, 130.16, 128.98, 128.64, 128.36, 127.28, 69.03, 52.50, 42.10, 41.14, 33.49, 32.82, 12.86. **HRMS-EI^{+}** (*m/z*): calc for $C_{23}H_{24}ClNO_3$ $[M]^{+}$ 397.1445, found 397.1448.

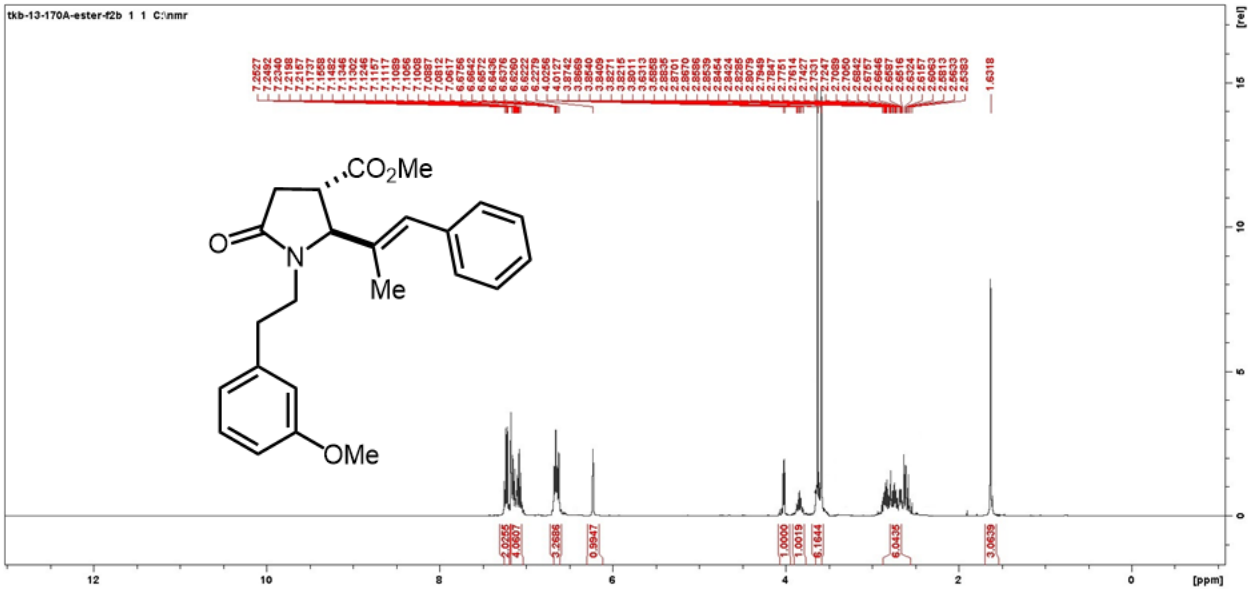


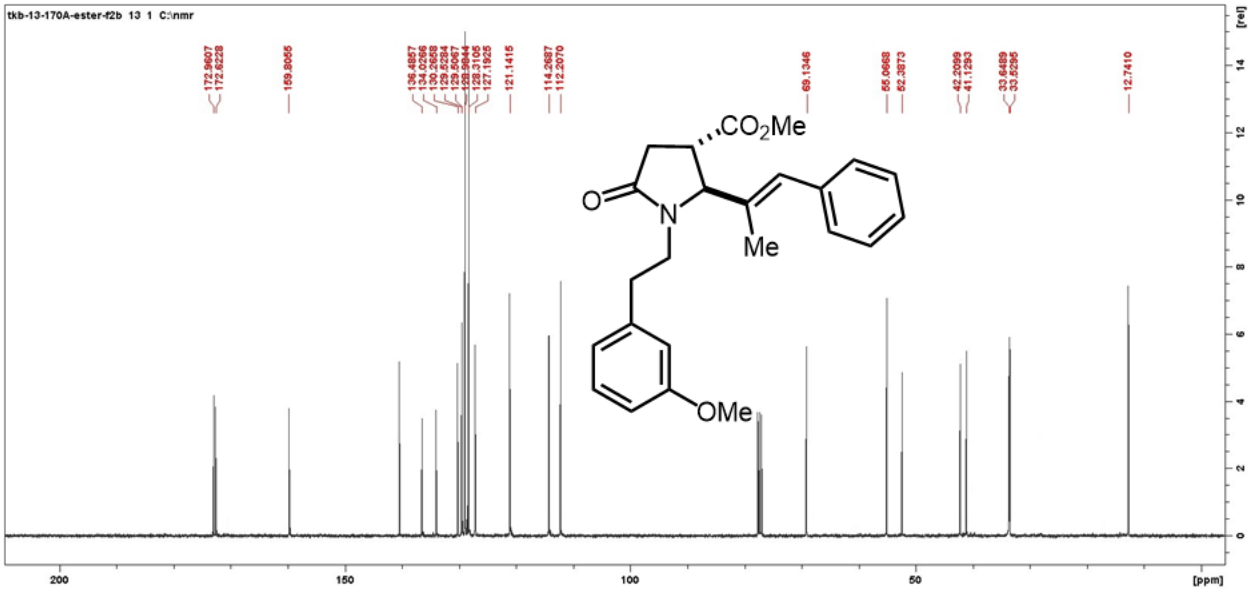


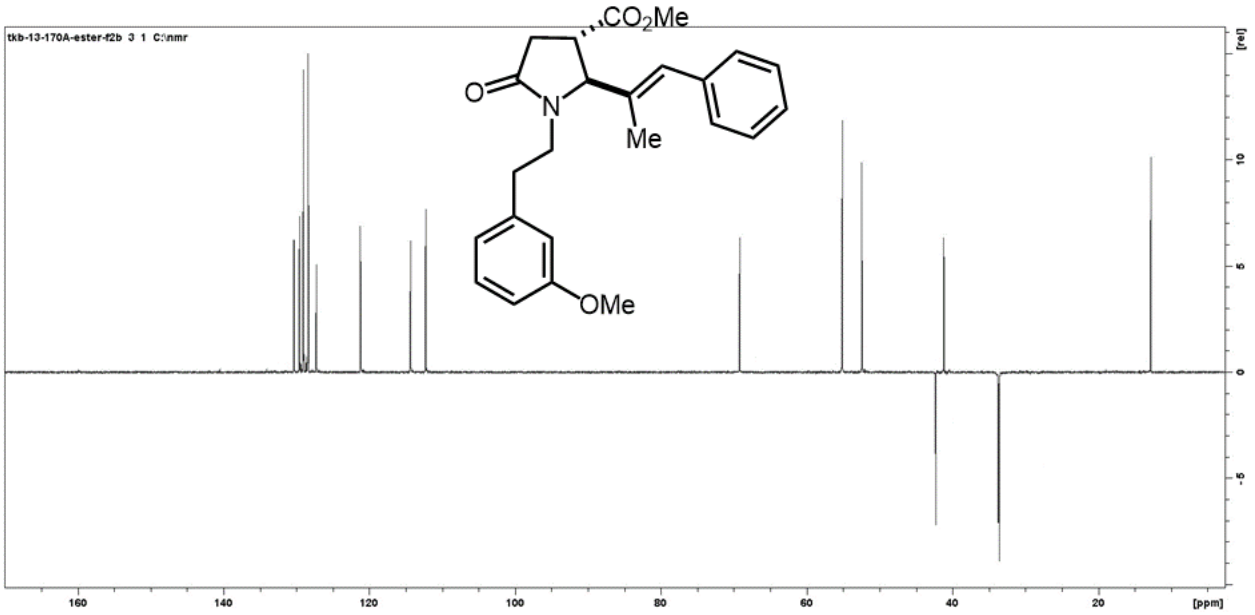
Compound 3t

Prepared in 1.0 mmol scale using **General Procedure A**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 50:50). Greenish-yellow oil. Yield = 334.5 mg, 85%, 95:5 dr (*trans:cis*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.06 (m, 6H), 6.72 – 6.57 (m, 3H), 6.23 (d, *J* = 1.8 Hz, 1H), 4.09 – 3.97 (m, 1H), 3.94 – 3.78 (m, 1H), 3.64 (s, 3H), 3.59 (s, 3H), 2.97 – 2.50 (m, 6H), 1.63 (d, *J* = 1.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.97, 172.63, 159.81, 140.46, 136.49, 134.03, 130.27, 129.53, 128.99, 128.31, 127.20, 121.15, 114.27, 112.21, 69.14,

55.07, 52.39, 42.21, 41.13, 33.65, 33.53, 12.74. **HRMS-EI$^+$** (*m/z*): calc for $C_{24}H_{27}NO_4$ $[M]^+$ 393.1940, found 393.1946.

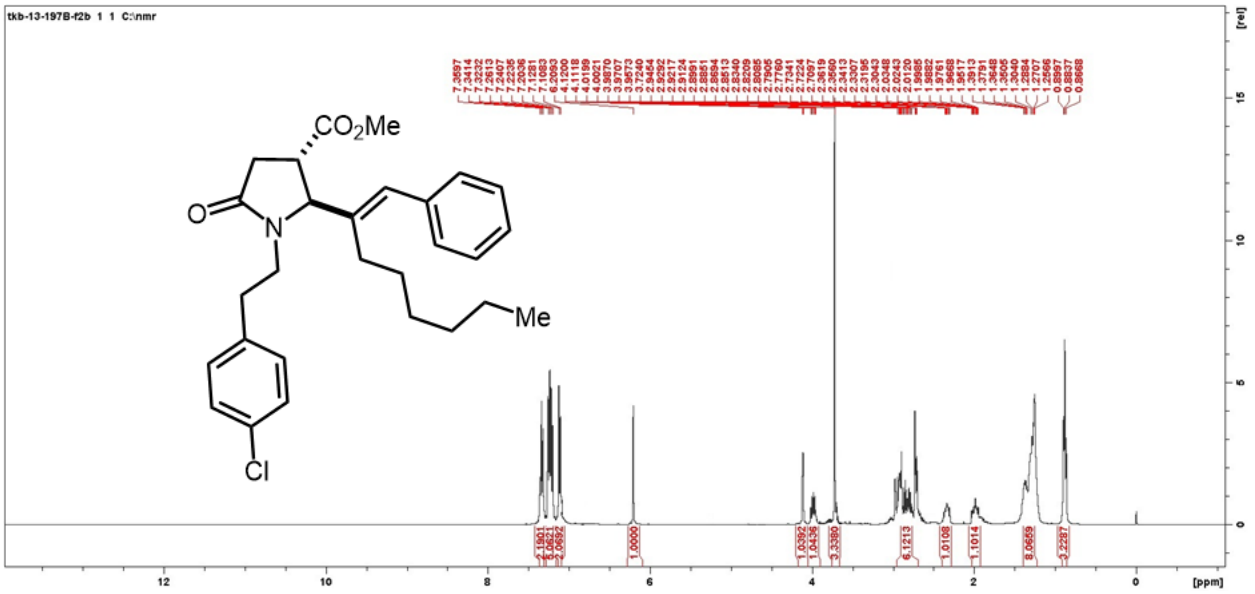






Compound 3u

Prepared in 1.0 mmol scale using **General Procedure A**. Purification: Flash chromatography on silica eluting with hexane/acetone (95:5 to 75:25). Greenish-yellow oil. Yield = 365.0 mg, 78%, 95:5 dr (*trans:cis*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.28 (m, 2H), 7.31 – 7.15 (m, 5H), 7.15 – 7.03 (m, 2H), 6.21 (s, 1H), 4.12 (d, J = 3.5 Hz, 1H), 3.99 (dt, J = 12.2, 6.3 Hz, 1H), 3.75 (s, 3H), 3.00 – 2.79 (m, 6H), 2.47 – 2.28 (m, 1H), 2.06 – 1.88 (m, 1H), 1.45 – 1.24 (m, 8H), 0.88 (t, J = 6.6 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.11, 173.08, 139.45, 137.33, 136.46, 132.29, 130.23, 128.66, 128.59, 128.55, 128.44, 128.40, 128.35, 127.33, 127.13, 66.43, 52.51, 42.48, 42.43, 33.05, 32.69, 31.34, 29.54, 28.55, 28.39, 22.52, 14.02. **HRMS-EI^{+}** (*m/z*): calc for $C_{28}H_{34}ClNO_3$ $[M]^{+}$ 467.2227, found 467.2223.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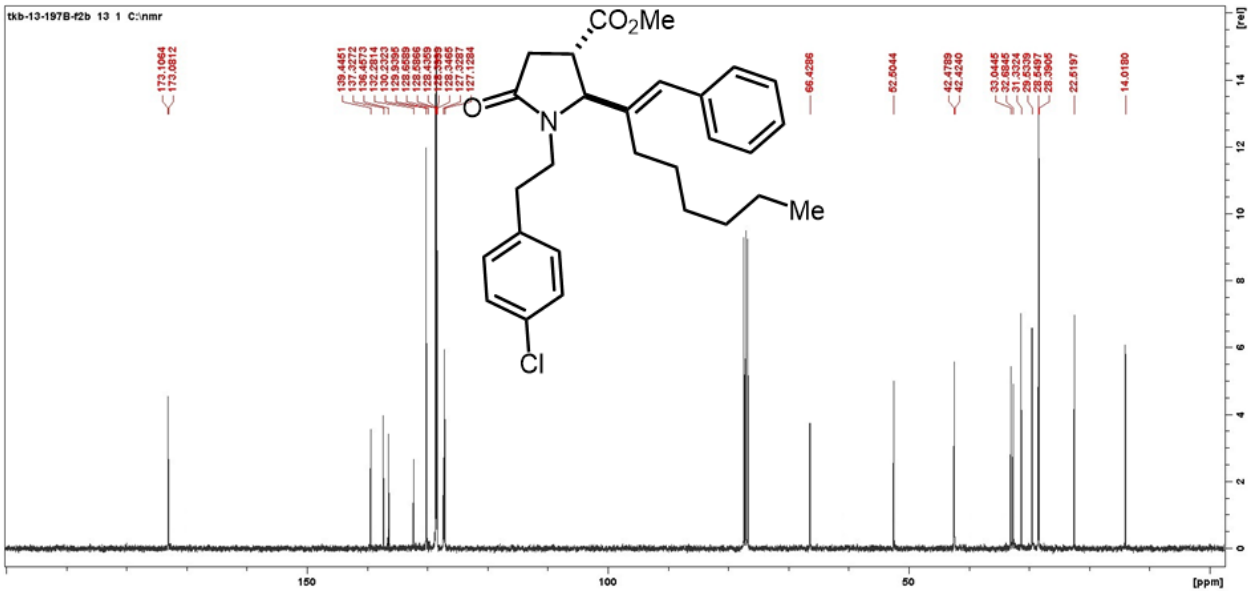
O
N
Me
Cl
[ppm]
[rel]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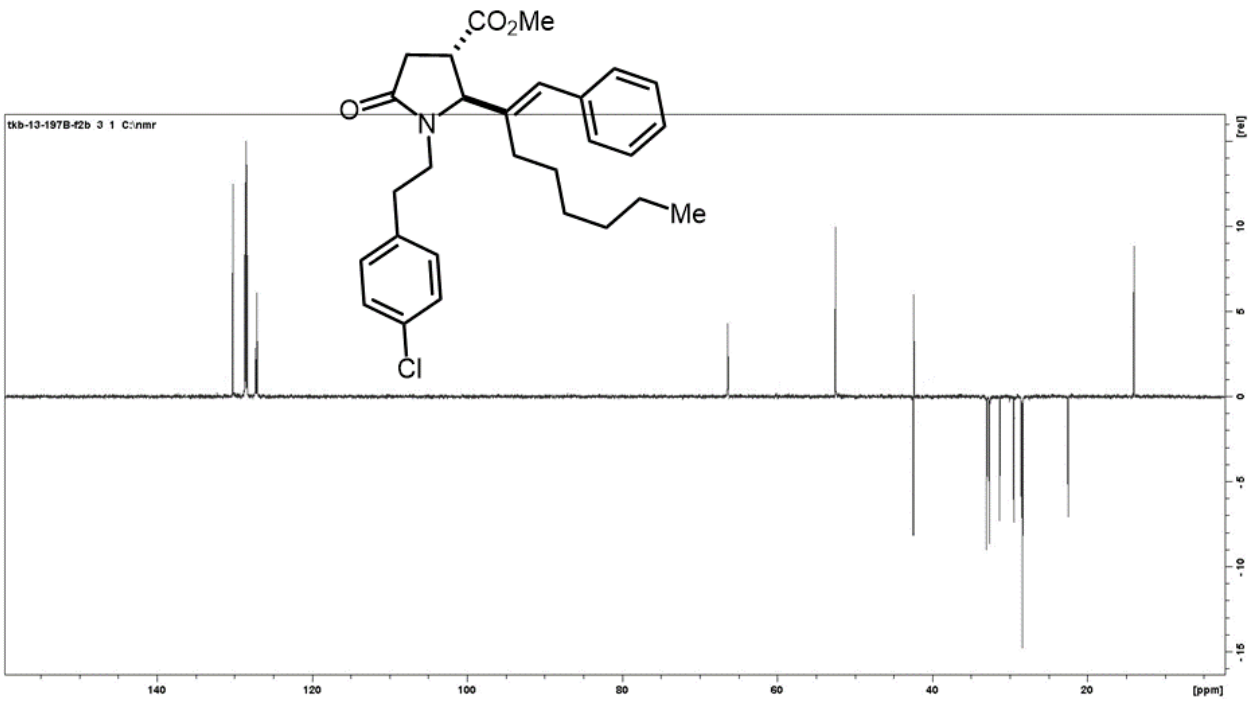
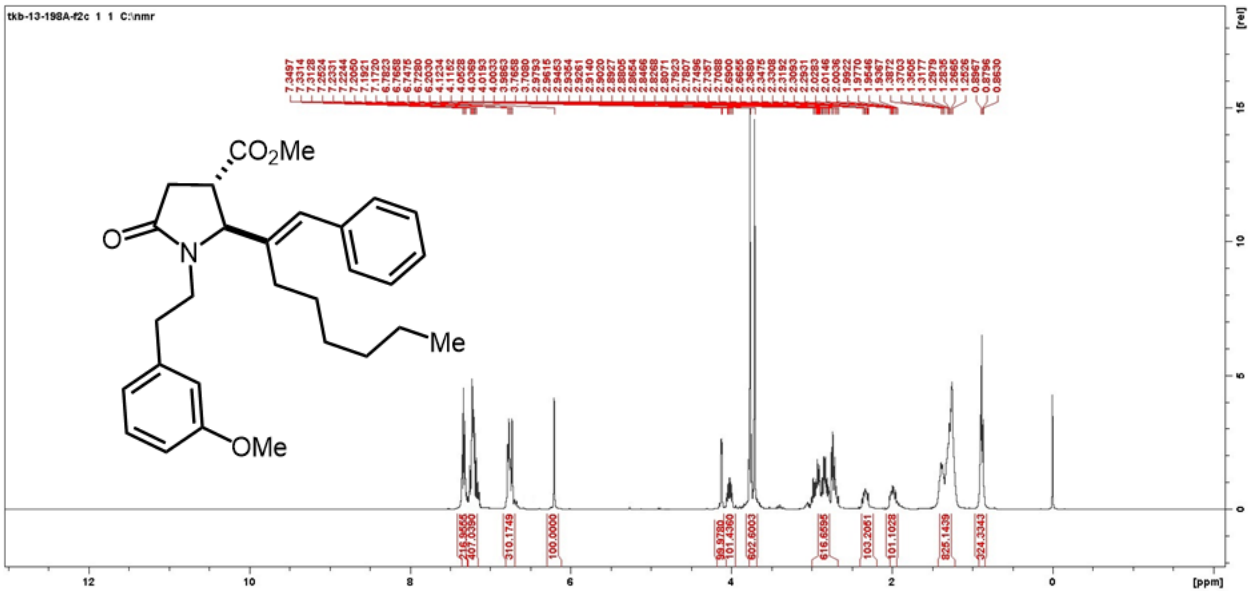
O
N
Me
Cl
[ppm]
[rel]



Compound 3v

Prepared in 1.0 mmol scale using **General Procedure A**. Purification: Flash chromatography on silica eluting with hexane/acetone (95:5 to 75:25). Greenish-yellow oil. Yield = 373.5 mg, 81%, 95:5 dr (*trans:cis*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.26 (m, 2H), 7.29 – 7.18 (m, 4H), 6.82 – 6.63 (m, 3H), 6.20 (s, 1H), 4.12 (d, J = 3.5 Hz, 1H), 4.02 (ddd, J = 13.3, 7.6, 5.7 Hz, 1H), 3.76 (s, 3H), 3.70 (s, 3H), 3.09 – 2.62 (m, 6H), 2.33 (ddd, J = 13.5, 9.9, 6.8 Hz, 1H), 2.05 – 1.87 (m, 1H), 1.35 – 1.19 (m, 8H), 0.87 (t, J = 6.5 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.06, 173.03, 159.81, 140.49, 139.55, 136.56, 129.52, 128.56, 128.37, 127.06, 121.08, 114.24, 112.19, 66.55, 55.07, 52.42, 42.59, 42.43, 33.85, 32.76, 31.32, 29.56, 28.51, 28.36, 22.52, 14.03. **HRMS-EI^{+}** (*m/z*): calc for $C_{29}H_{37}NO_4$ $[M]^+$ 463.2723, found 463.2729.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Me
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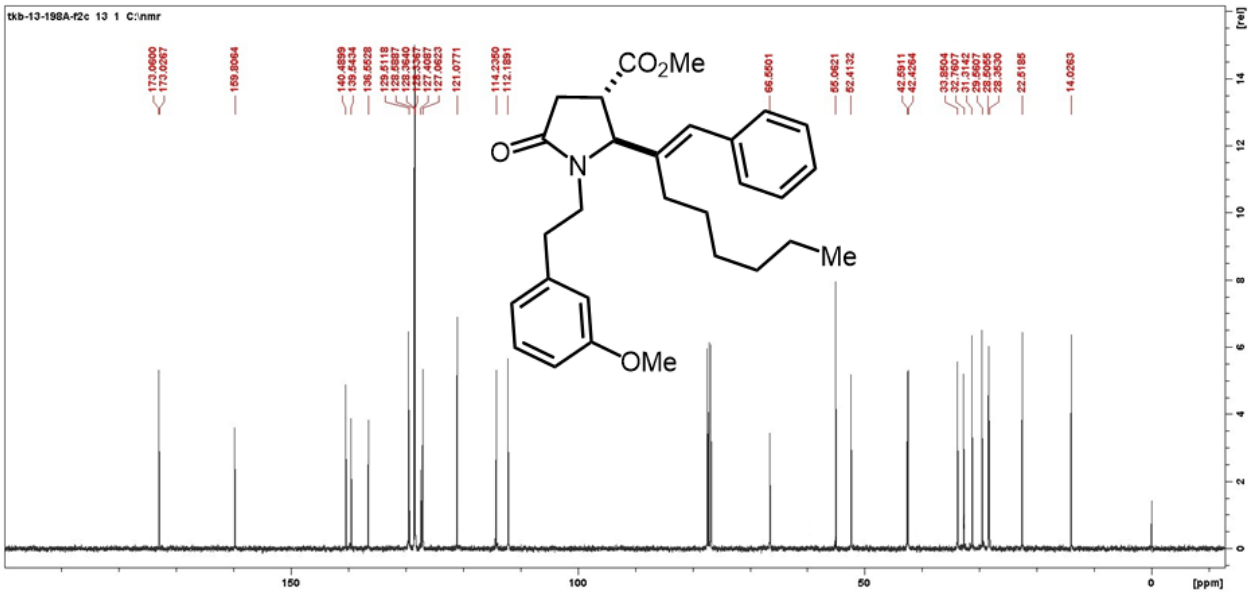
[ppm]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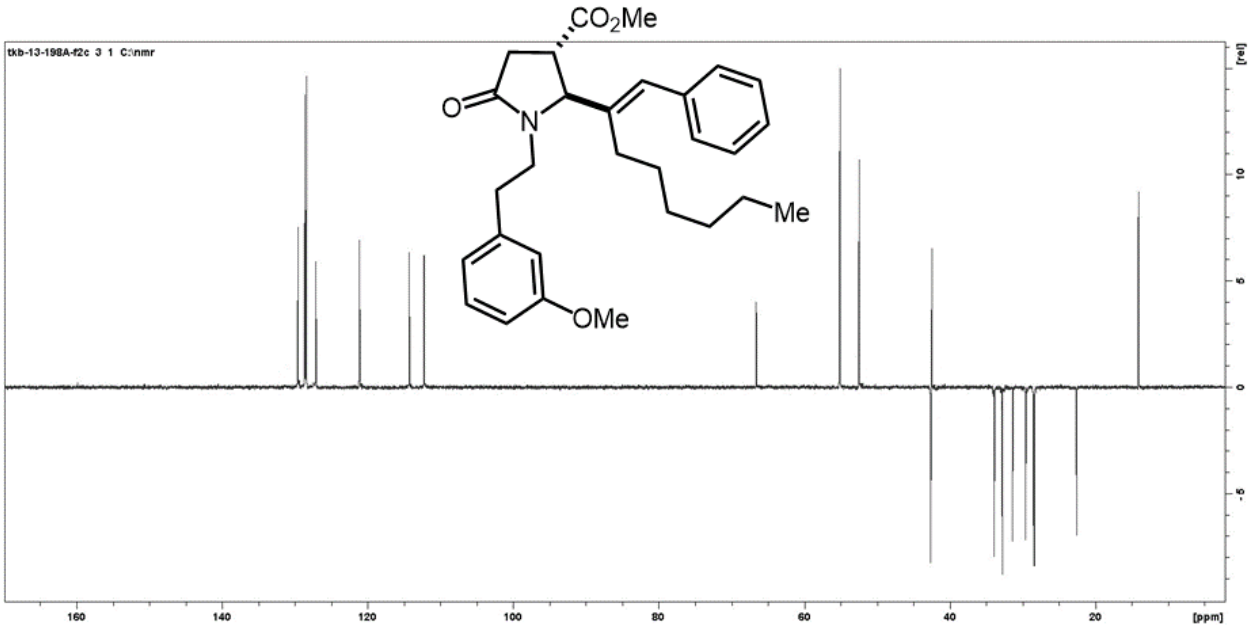
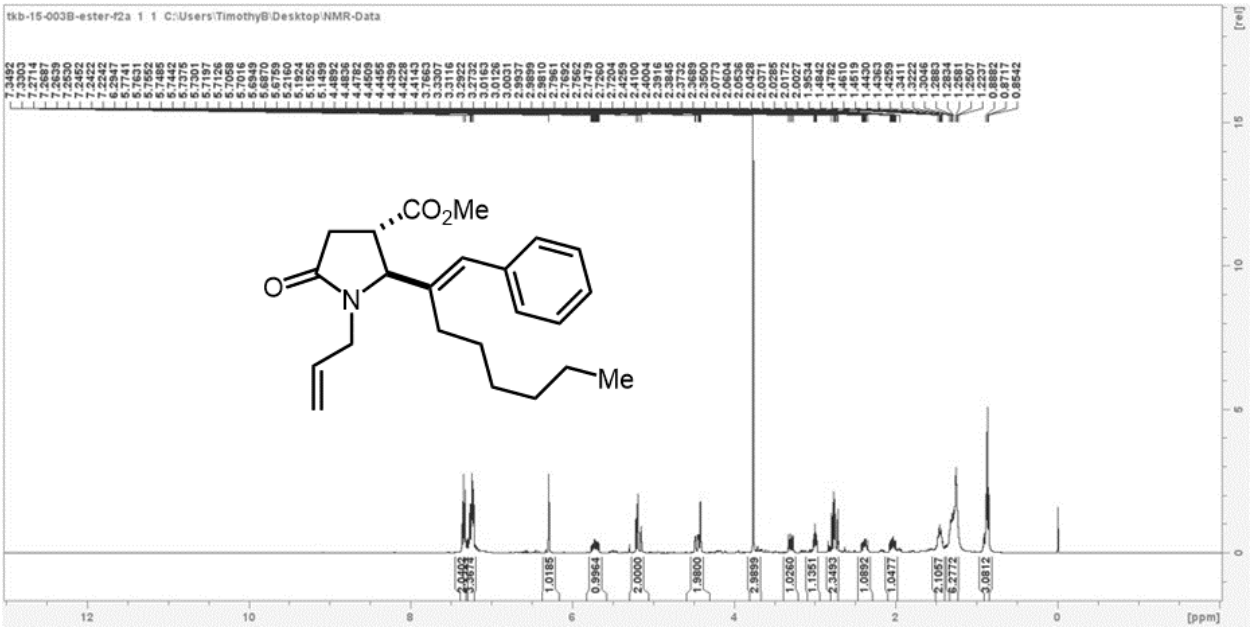
O
N
Me
OMe
[rel]
[ppm]



Compound 3w

Prepared in 1.0 mmol scale using **General Procedure A**. Purification: Flash chromatography on silica eluting with hexane/acetone (95:5 to 75:25). Greenish-yellow oil. Yield = 280.2 mg, 76%, 95:5 dr (*trans:cis*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.27 (m, 2H), 7.30 – 7.15 (m, 3H), 6.29 (s, 1H), 5.73 (dddd, *J* = 17.5, 10.3, 7.6, 4.4 Hz, 1H), 5.24 – 5.12 (m, 2H), 4.52 – 4.42 (m, 1H), 4.42 (d, *J* = 3.5 Hz, 1H), 3.77 (s, 3H), 3.35 – 3.25 (m, 1H), 3.11 – 2.96 (m, 1H), 2.86 – 2.67 (m, 2H), 2.39 (ddd, *J* = 13.8, 9.8, 6.8 Hz, 1H), 2.10 – 1.91 (m, 1H), 1.54 – 1.36 (m, 2H), 1.40 – 1.22 (m, 6H), 0.87 (t, *J* = 6.7 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.44, 172.81, 139.30, 136.59, 131.90, 128.55, 128.39, 127.37, 127.08, 118.23, 65.26, 52.55, 43.47, 42.58, 33.12, 31.37, 29.58, 28.88, 28.51, 22.52, 14.01. **HRMS-EI^{+}** (*m/z*): calc for $C_{23}H_{31}NO_3$ $[M]^+$ 369.2304, found 369.2308.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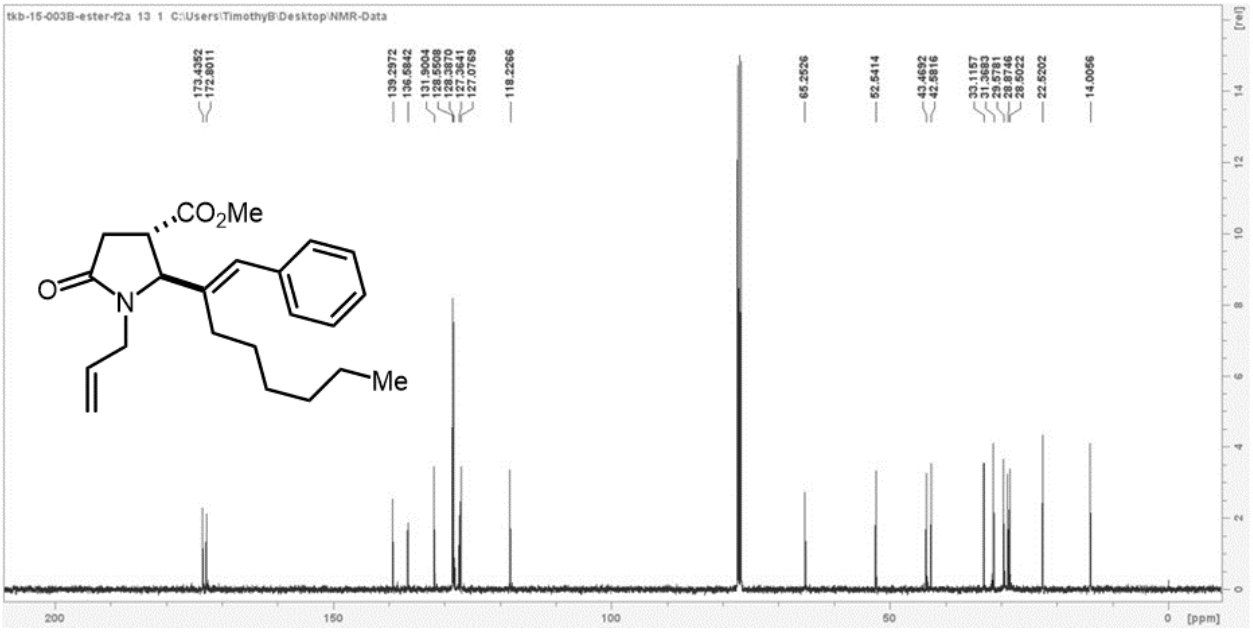
O
N
Me
[ppm]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118.2266
65.2526
52.5414
43.4692
42.5816
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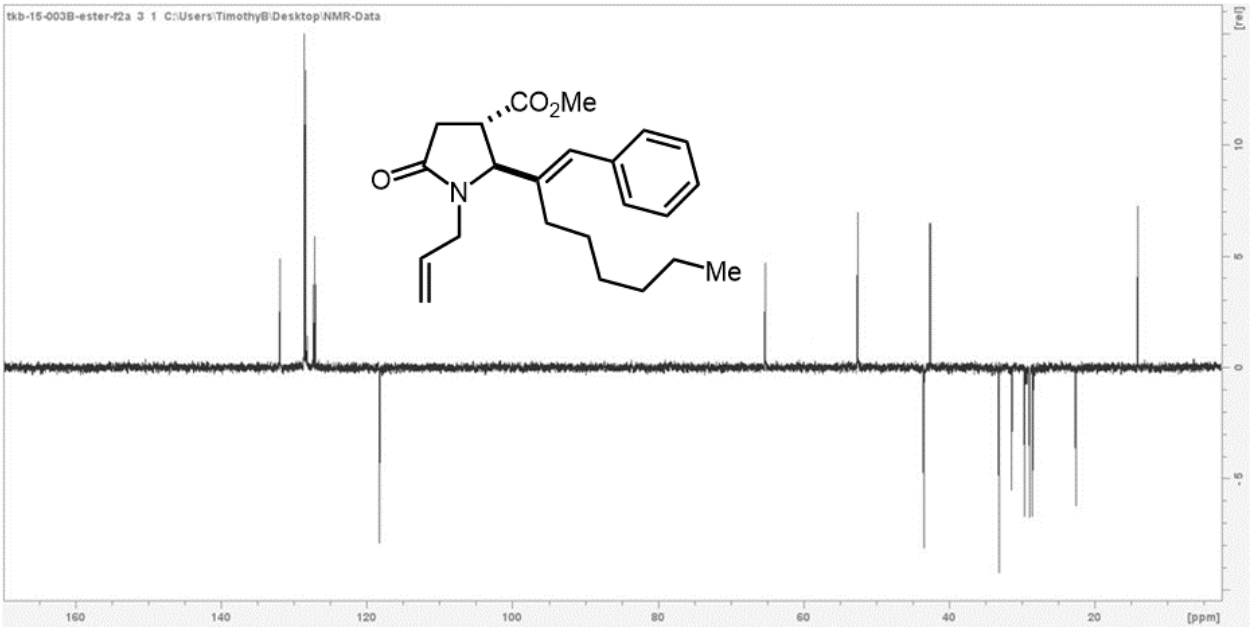
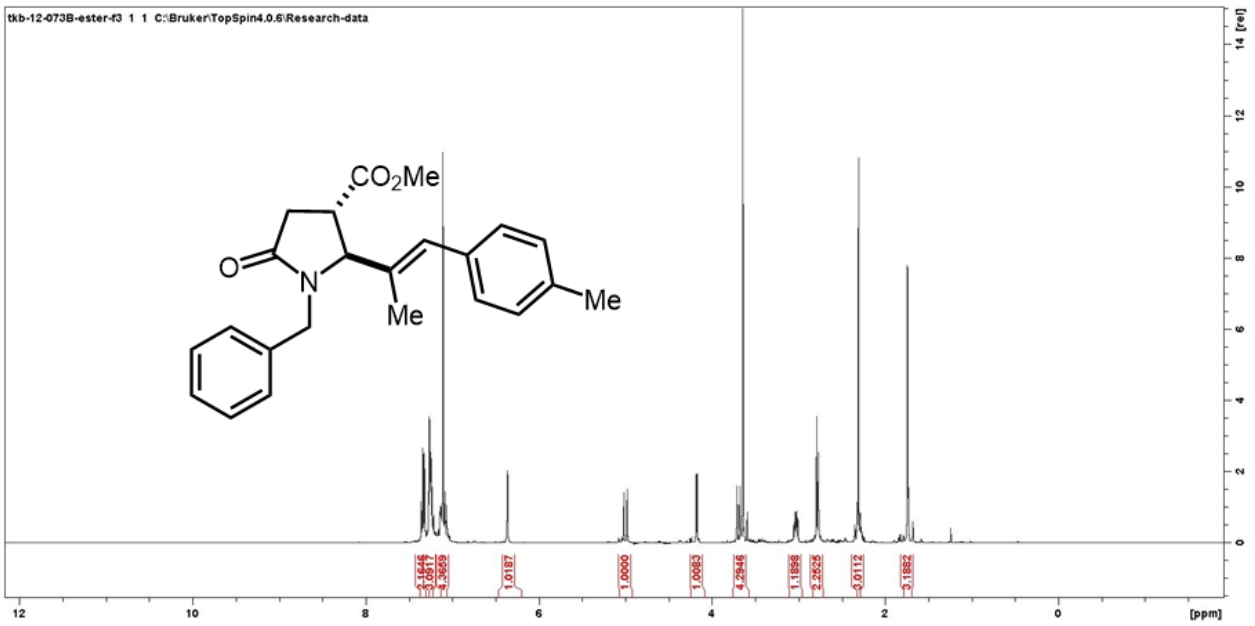
CO2Me
O
N
Me
[ppm]



Compound 3x

Prepared in 1.0 mmol scale using **General Procedure A**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 70:30). Amorphous solid. Yield = 308.9 mg, 85%, 95:5 dr (*trans:cis*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (dd, *J* = 8.1, 6.9 Hz, 2H), 7.14 – 7.04 (m, 3H), 7.08 – 6.96 (m, 4H), 6.19 (d, *J* = 1.5 Hz, 1H), 4.93 (d, *J* = 14.7 Hz, 1H), 4.01 (d, *J* = 5.2 Hz, 1H), 3.52 (d, *J* = 14.7 Hz, 1H), 3.47 (s, 3H), 3.40 (dd, *J* = 26.1, 12.7 Hz, 1H), 2.69 – 2.53 (m, 2H), 2.12 (s, 3H), 1.56 (dd, *J* = 4.7, 1.5 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.14, 172.83, 137.29, 136.63, 133.86, 133.04, 130.49, 129.35, 129.33, 129.06, 128.95, 128.53, 128.51, 128.40, 127.26, 68.09, 52.46, 44.43, 41.10, 33.79, 28.26, 21.23, 12.92. **HRMS-EI^{+}** (*m/z*): calc for $C_{23}H_{25}NO_3$ $[M]^{+}$ 363.1834, found 363.1839.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N
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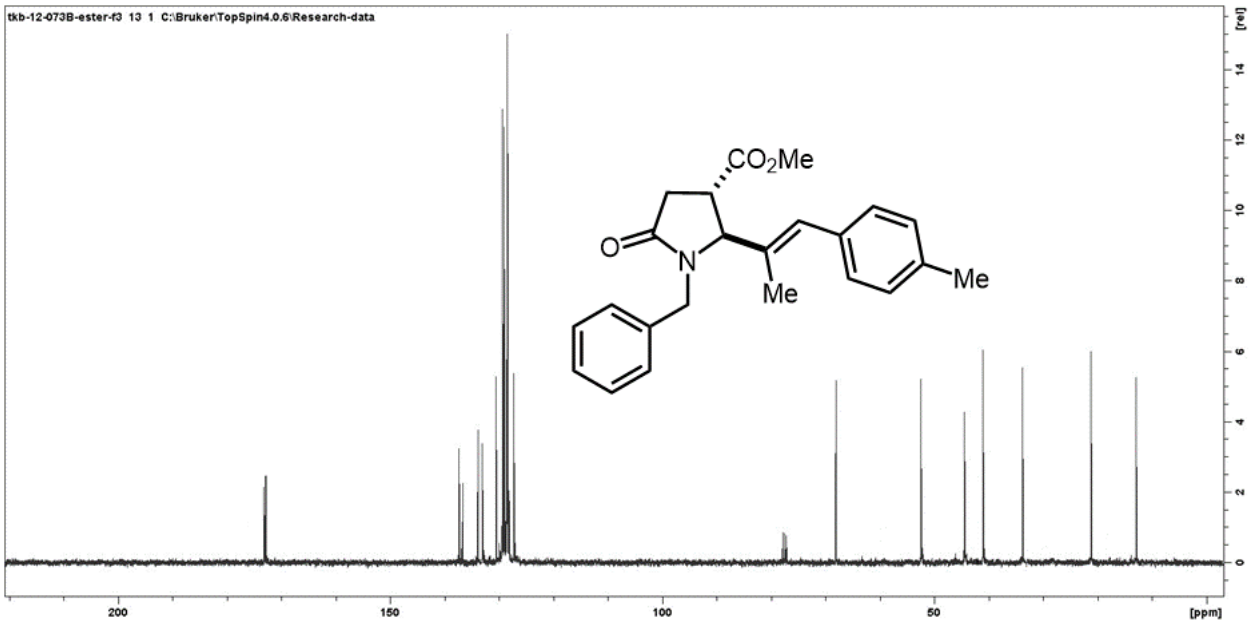
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Me
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150
100
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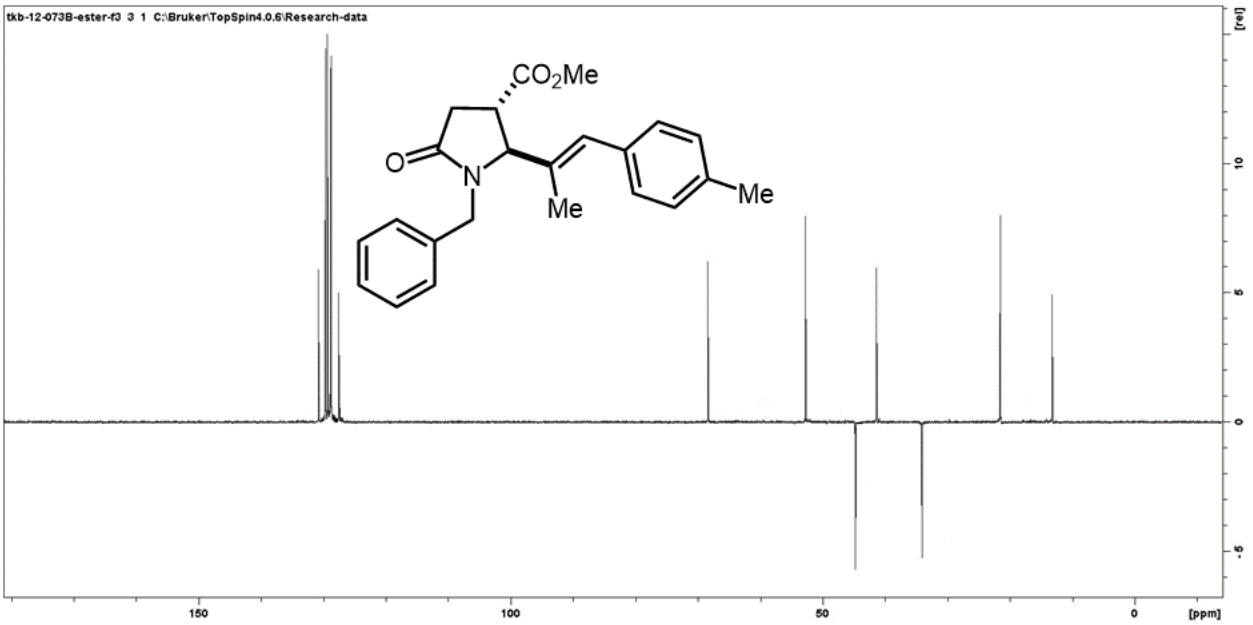
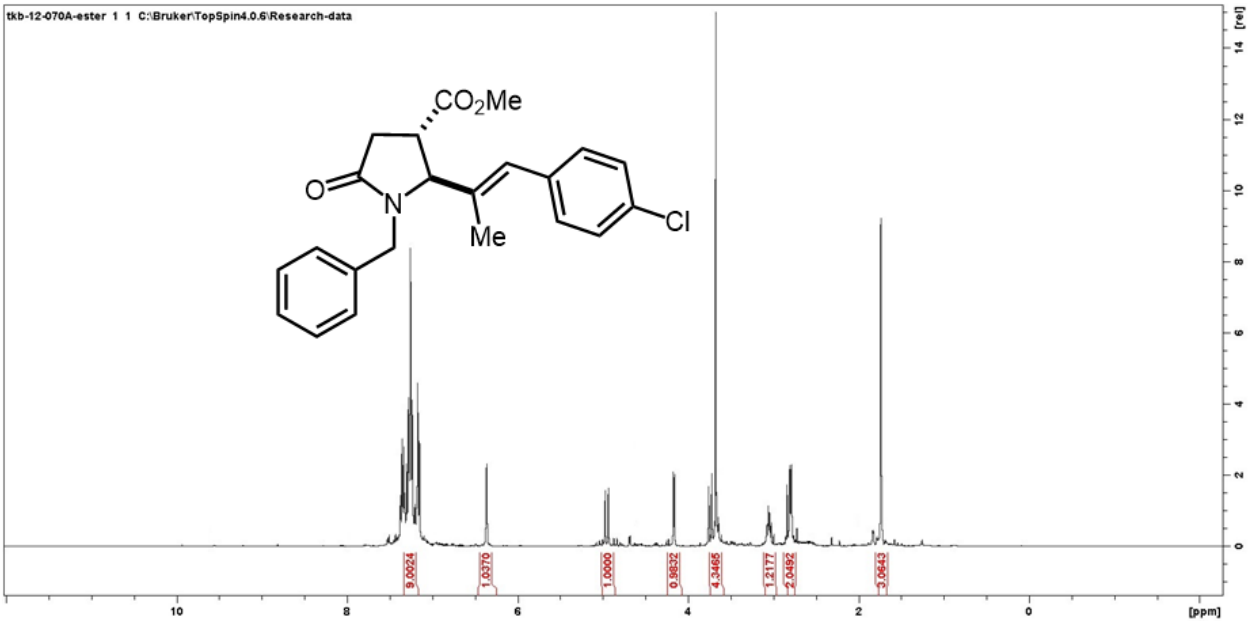
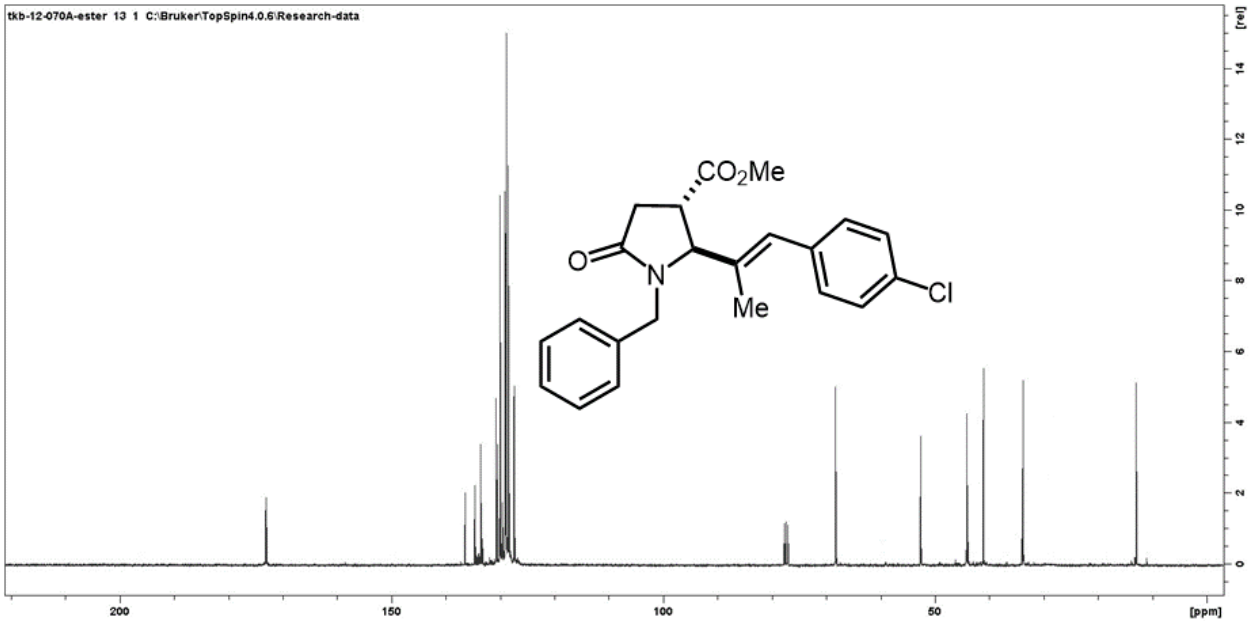
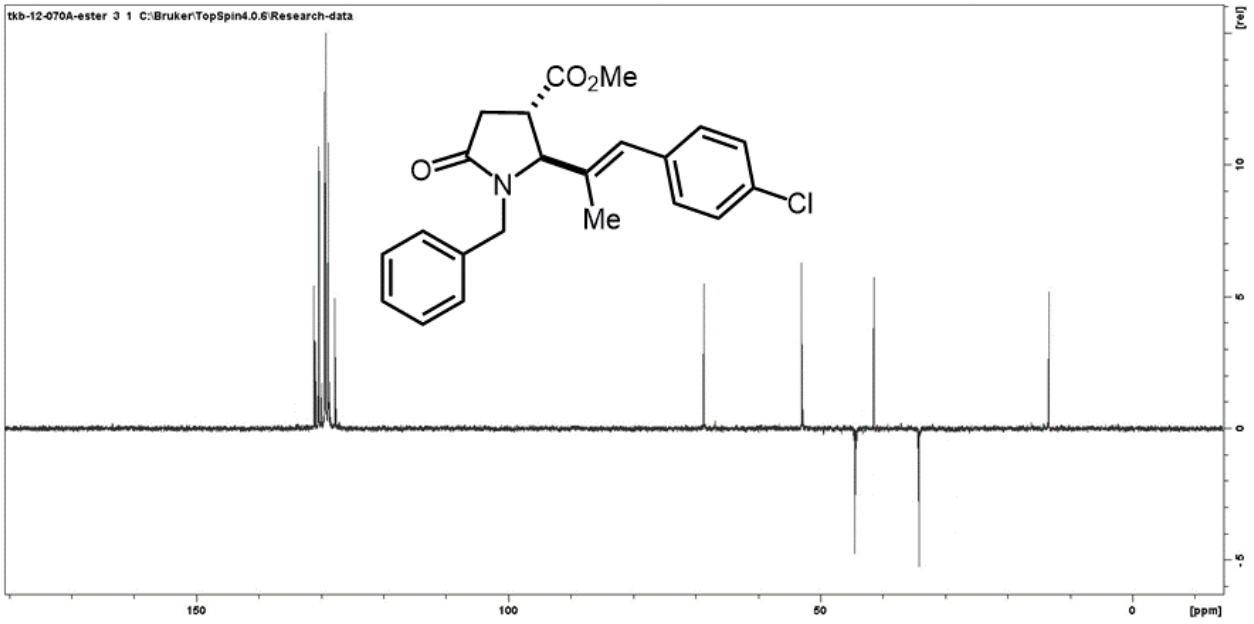


Compound 3y

Prepared in 1.0 mmol scale using **General Procedure A**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 70:30). Amorphous solid. Yield = 303.3 mg, 79%, 95:5 dr (*trans:cis*).^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.12 (m, 9H), 6.39 (s, 1H), 4.89 (d, J = 15.2 Hz, 1H), 4.19 (d, J = 5.2 Hz, 1H), 3.71 – 3.65 (m, 4H), 3.16 – 3.00 (m, 1H), 2.82 (dt, J = 7.9, 3.2 Hz, 2H), 1.77 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.10, 172.98, 136.39, 134.65, 133.55, 130.72, 130.48, 129.94, 129.03, 128.85, 128.45, 127.39, 68.26, 52.59, 44.10, 41.06, 33.75, 28.29, 12.94. **HRMS-EI**$^{+}$ (*m/z*): calc for $C_{22}H_{22}ClNO_3$ $[M]^+$ 383.1288, found 383.1284.



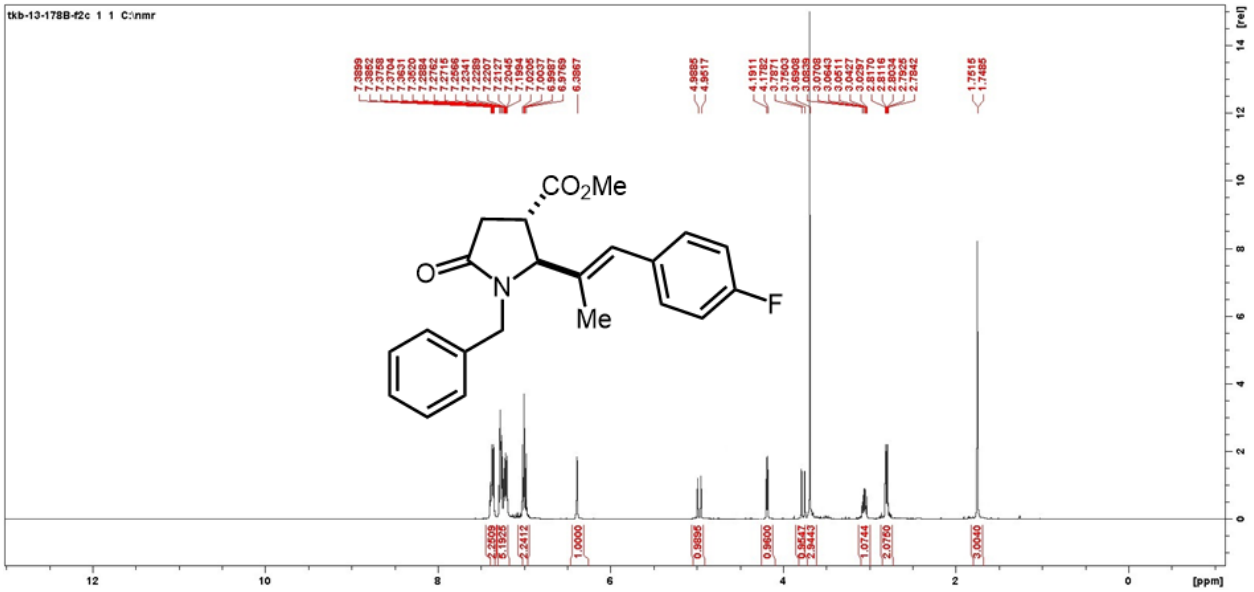


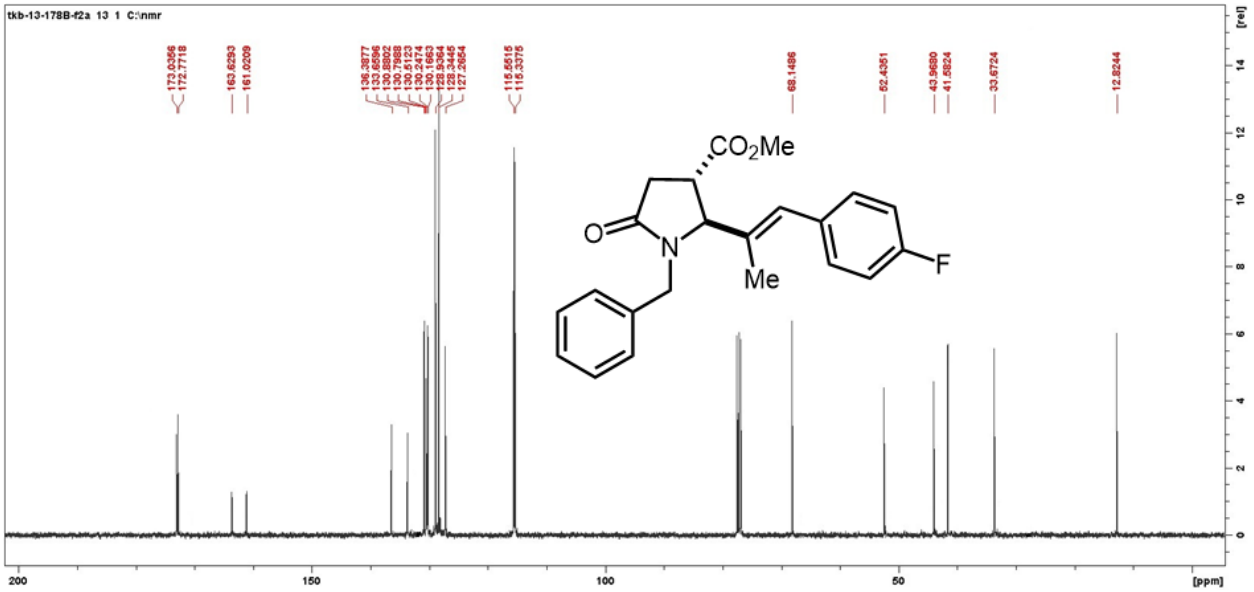


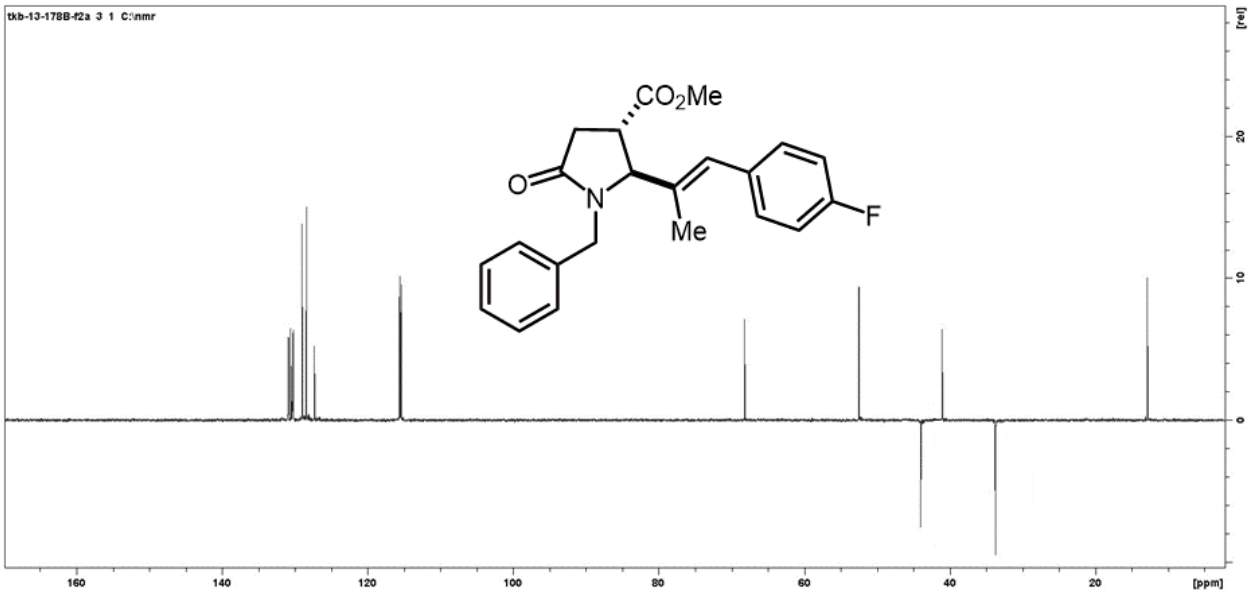
Compound 3z

Prepared in 1.0 mmol scale using **General Procedure A**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 70:30). Amorphous solid. Yield = 275.6 mg, 75%, 95:5 dr (*trans:cis*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.32 (m, 2H), 7.32 – 7.15 (m, 5H), 7.03 – 6.97 (m, 2H), 6.39 (d, *J* = 1.5 Hz, 1H), 4.97 (d, *J* = 14.7 Hz, 1H), 4.18 (d, *J* = 5.2 Hz, 1H), 3.77 (d, *J* = 14.7 Hz, 1H), 3.69 (s, 3H), 3.13 – 3.00 (m, 1H), 2.86 – 2.73 (m, 2H), 1.75 (d, *J* = 1.5 Hz,

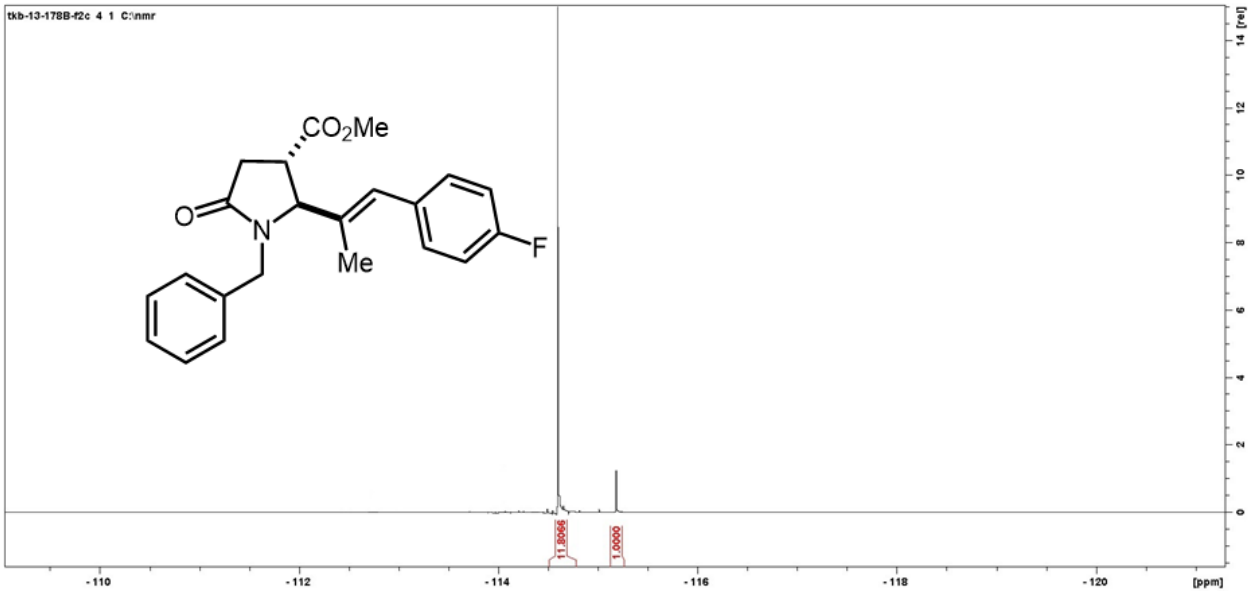
3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.04, 172.79, 163.49, 161.04, 136.39, 133.64, 130.55, 130.26, 130.18, 128.94, 128.36, 127.28, 115.57, 115.36, 68.16, 52.45, 43.99, 41.05, 33.70, 28.19, 12.84. **HRMS-EI**$^+$ (*m/z*): calc for $C_{22}H_{22}FNO_3$ $[M]^+$ 367.1584, found 367.1589.







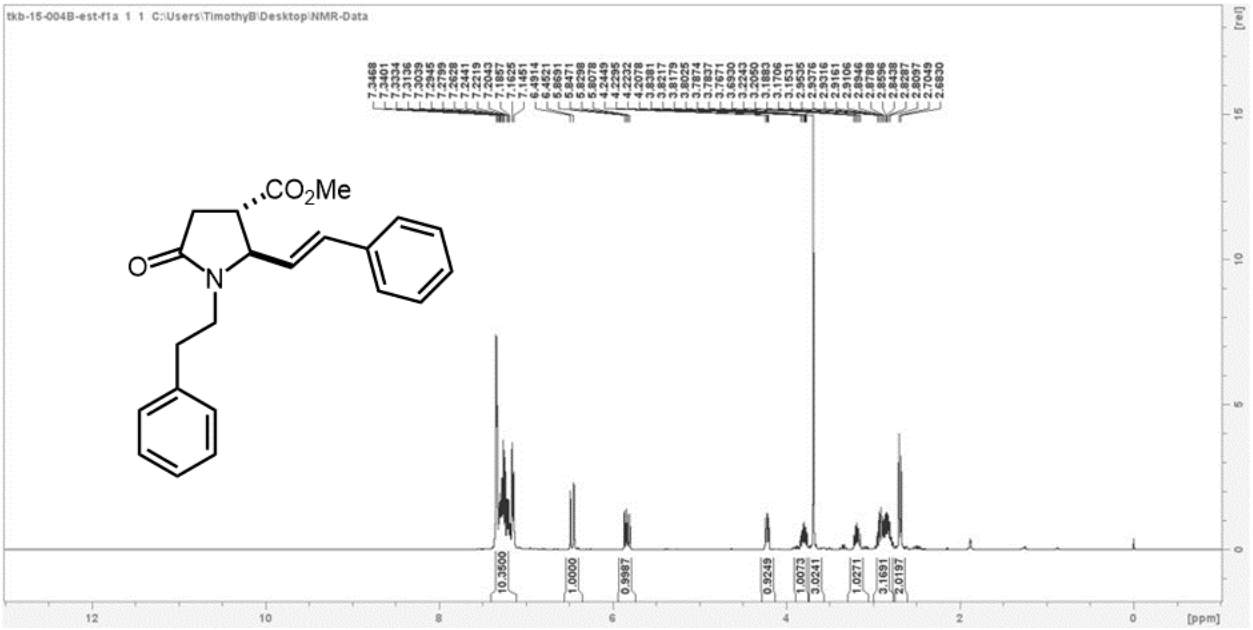
^{19}F NMR

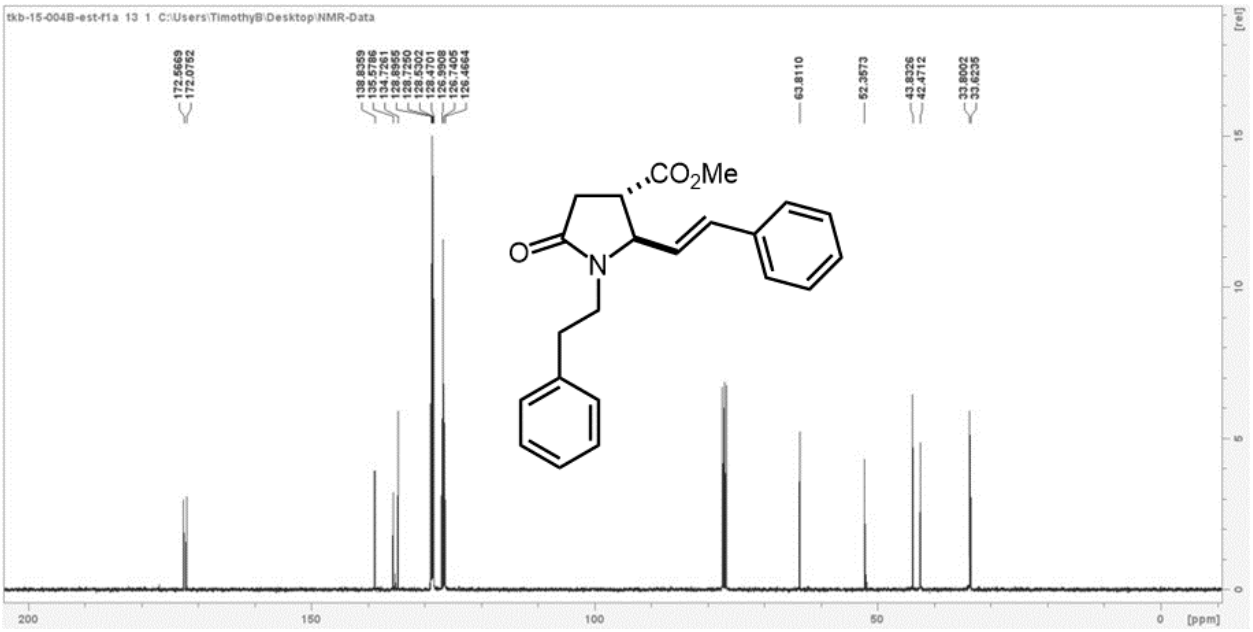


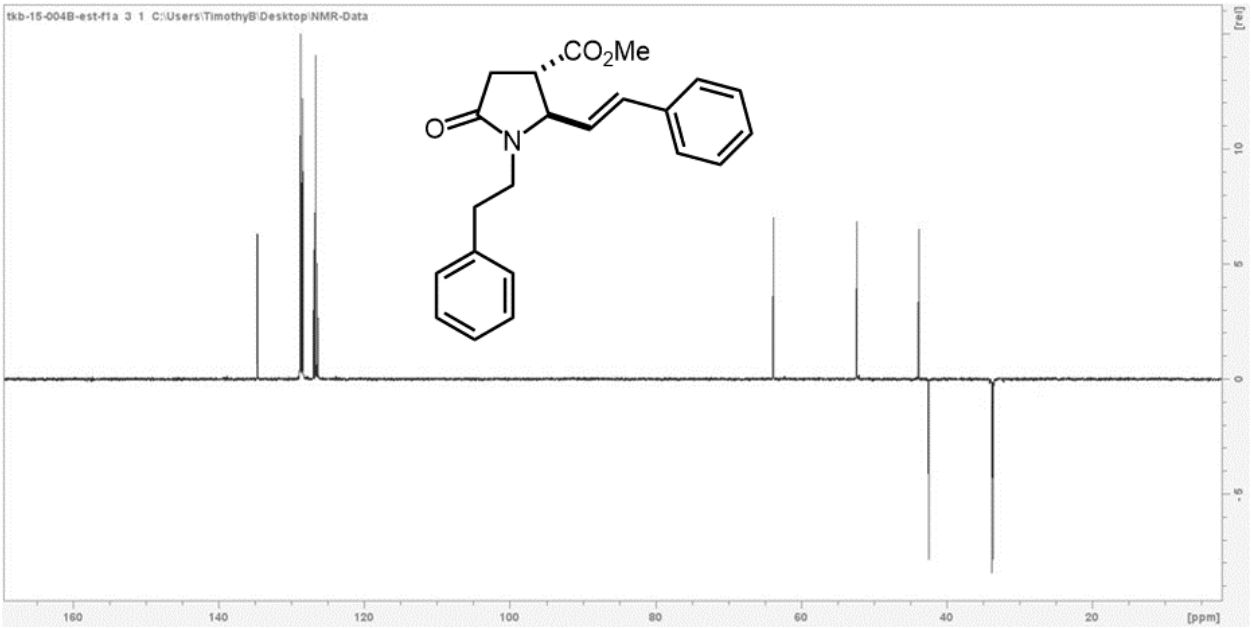
Compound 3z1

Prepared in 1.0 mmol scale using **General Procedure A**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 70:30). Greenish-yellow oil. Yield = 304.0 mg, 87%, 95:5 dr (*trans:cis*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.14 (m, 10H), 6.57 (d, J = 15.7 Hz, 1H), 5.92 (dd, J = 15.7, 8.9 Hz, 1H), 4.18 (hept, J = 7.0 Hz, 1H), 3.84 – 3.77 (m, 1H), 3.68 (s, 3H), 3.22 – 3.15 (m, 1H), 2.95 – 2.81 (m, 3H), 2.70 – 2.68 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.57,

172.08, 138.84, 135.58, 134.73, 128.90, 128.73, 128.53, 128.47, 126.99, 126.75, 126.47, 63.82, 52.36, 43.84, 42.47, 33.80, 33.63. **HRMS-EI$^+$** (*m/z*): calc for $C_{22}H_{23}NO_3$ $[M]^+$ 349.1678, found 349.1682.

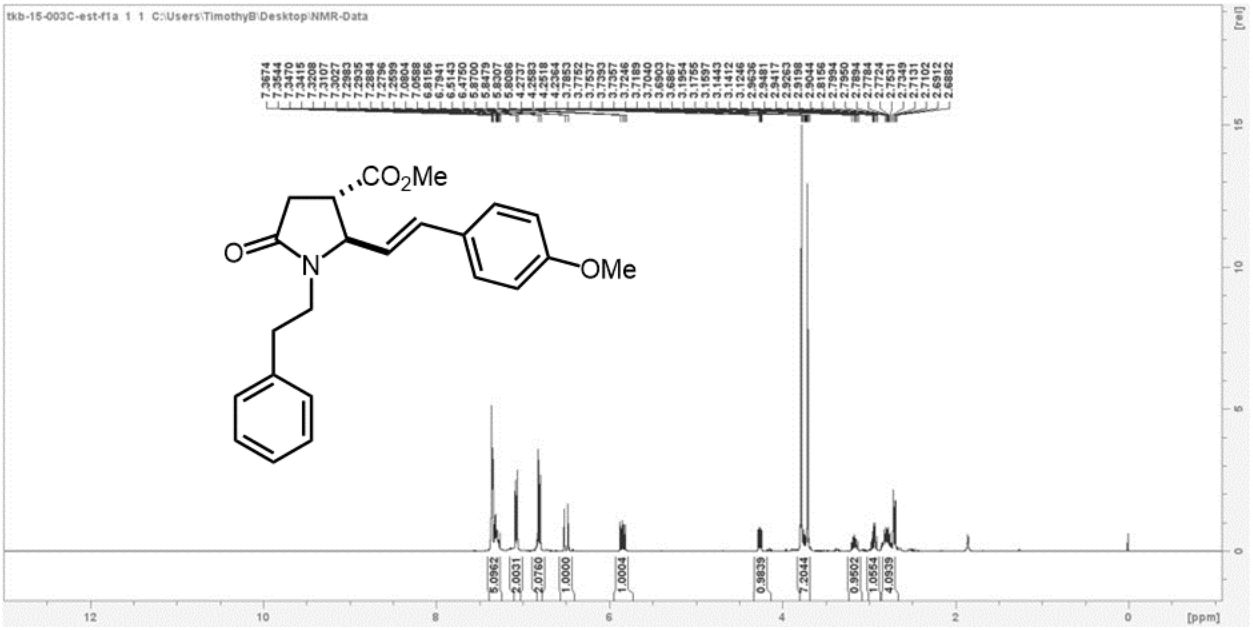






Compound 3*z*2

Prepared in 1.0 mmol scale using **General Procedure A**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 50:50). Greenish-yellow oil. Yield = 341.5 mg, 90%, 95:5 dr (*trans:cis*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.25 (m, 5H), 7.16 – 7.03 (m, 2H), 6.88 – 6.76 (m, 2H), 6.49 (d, *J* = 15.7 Hz, 1H), 5.84 (dd, *J* = 15.7, 8.9 Hz, 1H), 4.26 (dd, *J* = 8.8, 6.1 Hz, 1H), 3.78 (s, 3H), 3.81 – 3.70 (m, 1H), 3.70 (s, 3H), 3.16 (ddd, *J* = 14.0, 8.2, 6.4 Hz, 1H), 2.93 (td, *J* = 8.8, 6.1 Hz, 1H), 2.87 – 2.65 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.62, 172.11, 158.28, 135.55, 134.68, 130.80, 129.84, 129.82, 128.74, 128.48, 126.98, 126.74, 113.96, 63.83, 55.25, 52.41, 43.83, 42.69, 33.67, 32.86. **HRMS-EI^{+}** (*m/z*): calc for $C_{23}H_{25}NO_4$ $[M]^{+}$ 379.1784, found 379.1789.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O
N
OMe
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2.0760
1.0000
1.0004
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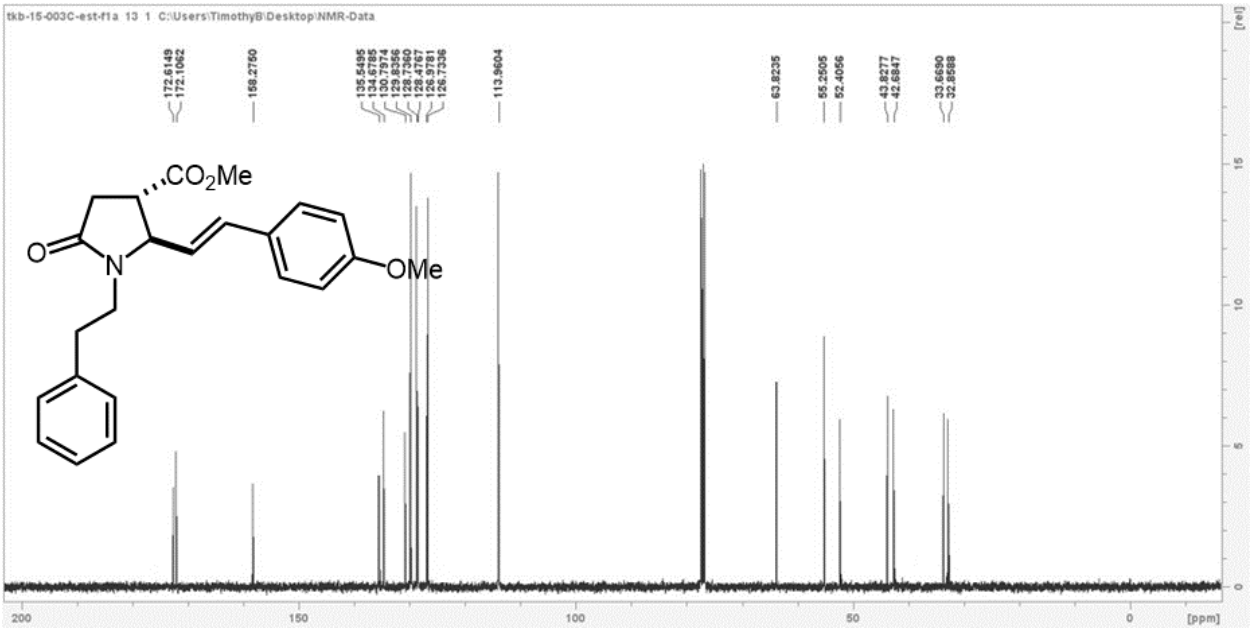
0.9502
1.0554
4.0939
12
10
8
6
4
2
0
[ppm]


tkb-15-003C-est-f1a 13 1 C:\Users\TimothyB\Desktop\NMR-Data
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CO2Me
O
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OMe
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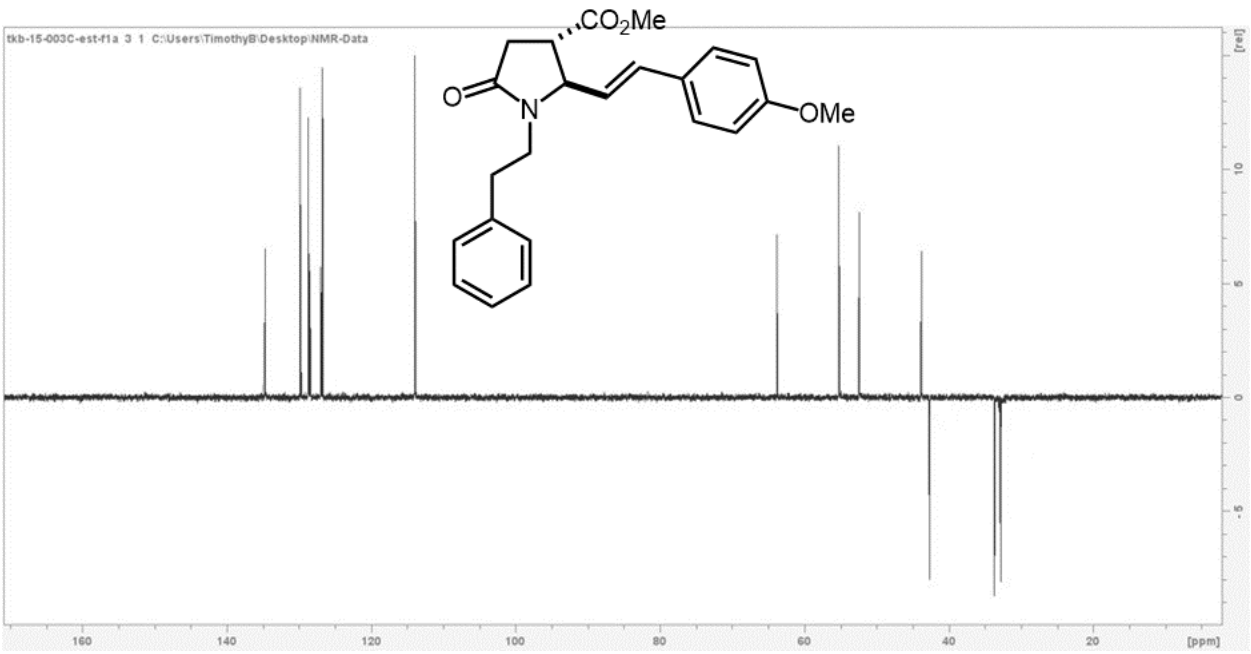
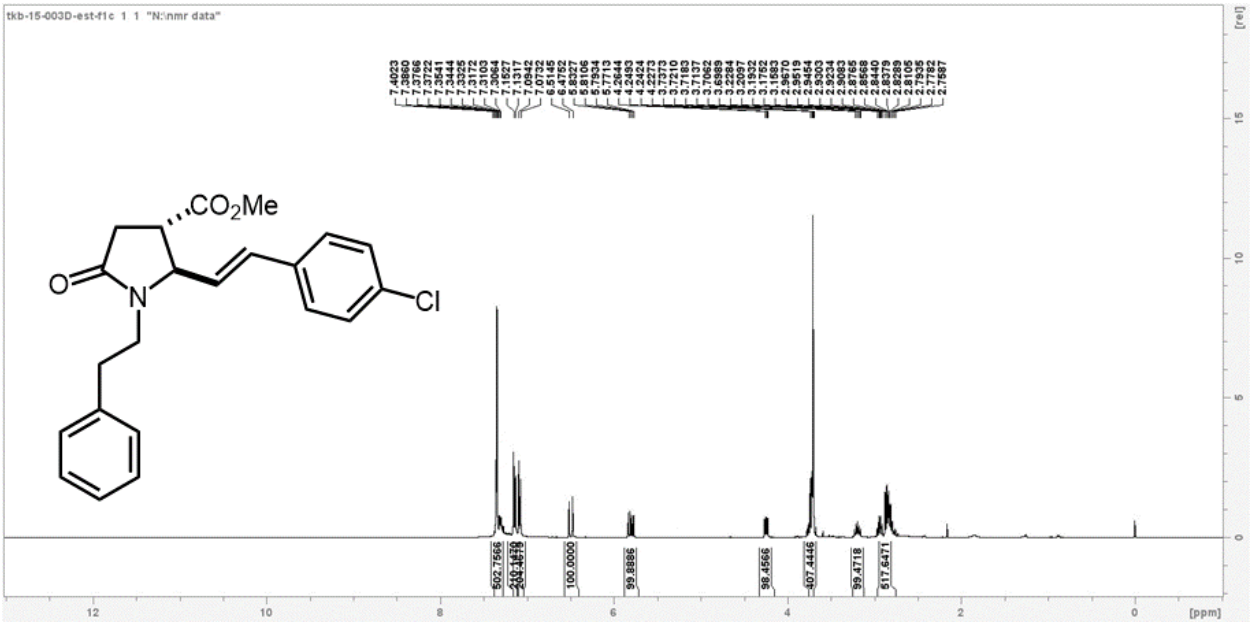
[ppm]



Compound 3z3

Prepared in 1.0 mmol scale using **General Procedure A**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 70:30). Greenish-yellow oil. Yield = 318.6 mg, 83%, 95:5 dr (*trans:cis*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.19 (m, 9H), 6.50 (d, *J* = 15.7 Hz, 1H), 5.80 (dd, *J* = 15.7, 8.8 Hz, 1H), 4.25 (dd, *J* = 8.8, 6.0 Hz, 1H), 3.80 – 3.65 (m, 4H), 3.19 (ddd, *J* = 14.0, 7.8, 6.3 Hz, 1H), 2.80 – 2.64 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.92, 172.55, 172.20, 137.26, 136.21, 135.40, 134.74, 132.56, 132.29, 130.27, 130.18, 128.77, 128.69, 128.65, 128.57, 126.77, 126.73, 63.87, 52.46, 43.77, 42.35, 33.12, 32.84. **HRMS-EI$^+$** (*m/z*): calc for $C_{22}H_{22}ClNO_3$ $[M]^+$ 383.1288, found 383.1294.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N
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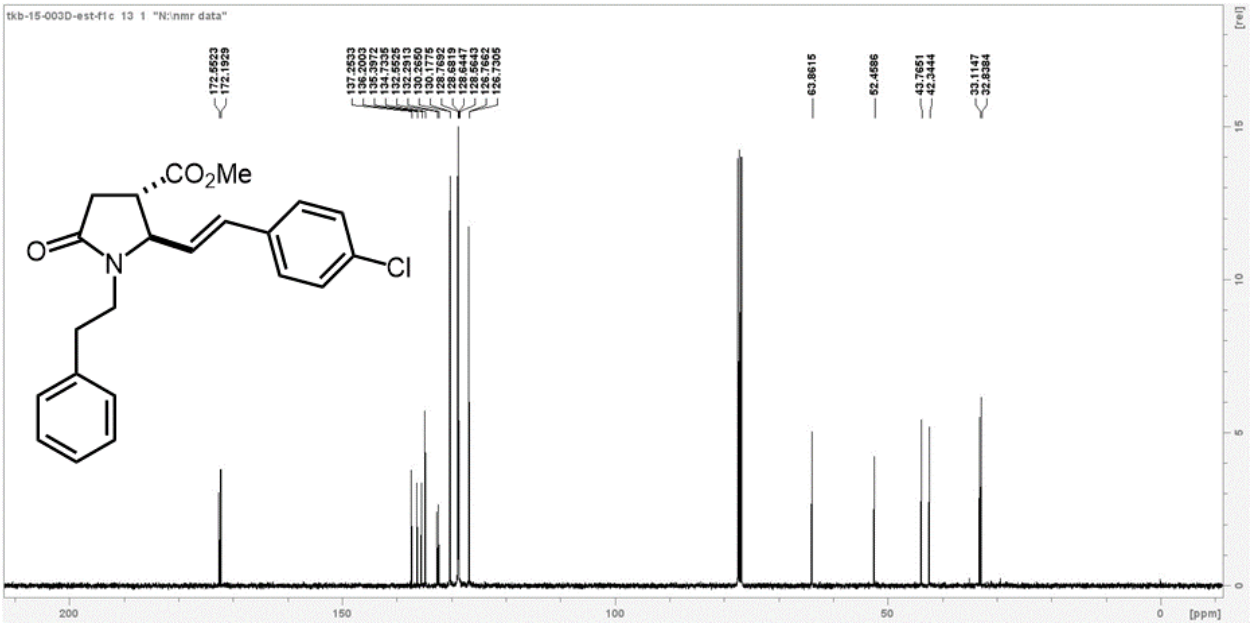
[ppm]


tkb-15-003D-est-f1c 13 1 "Nuclear Magnetic Resonance data"
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Cl
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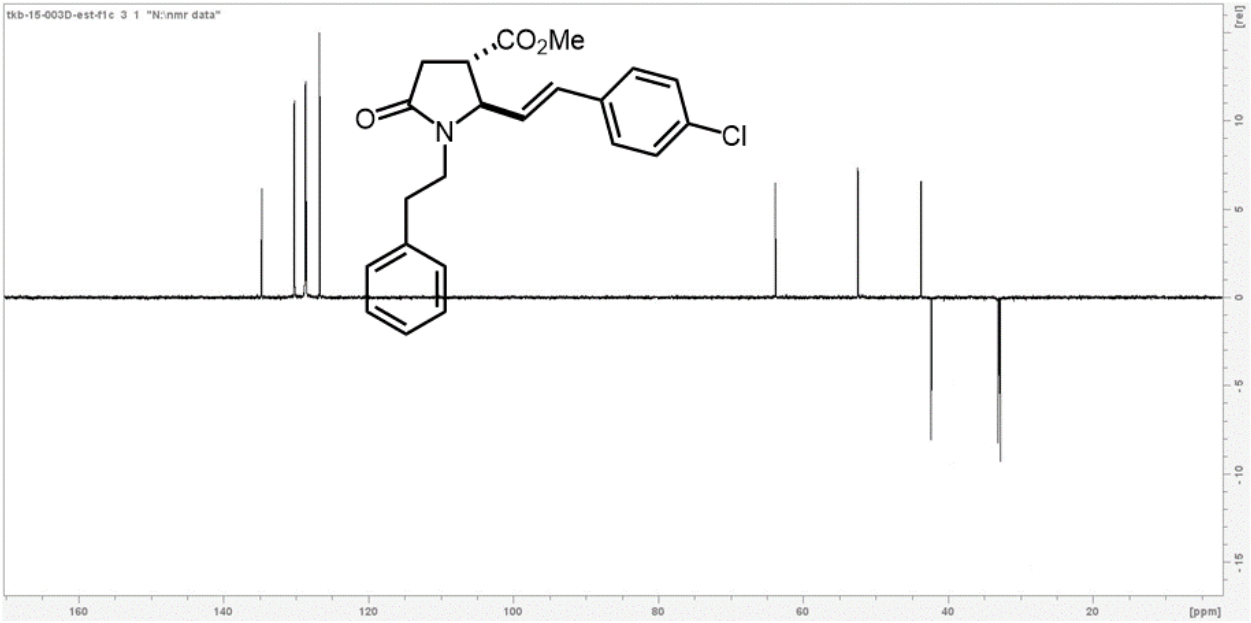
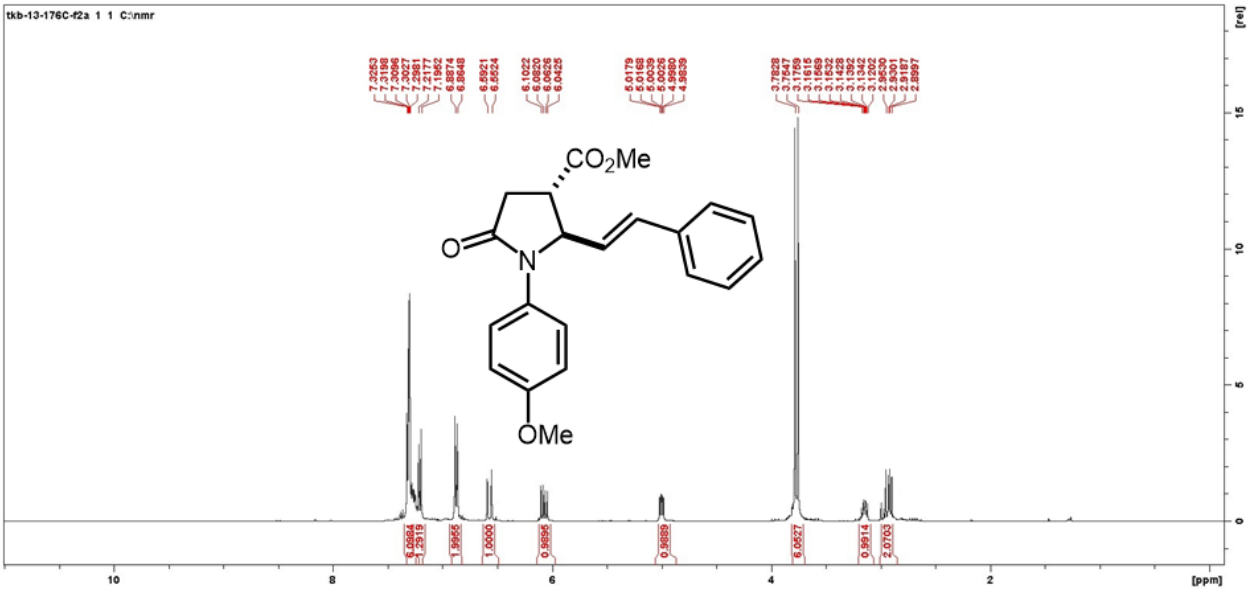
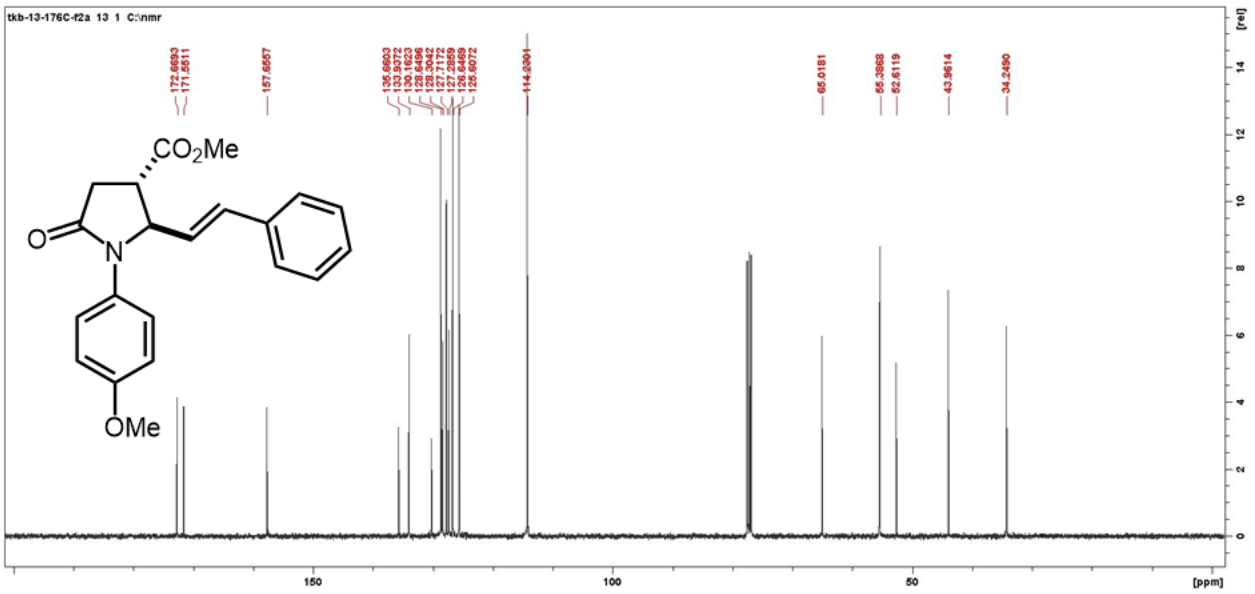
[ppm]

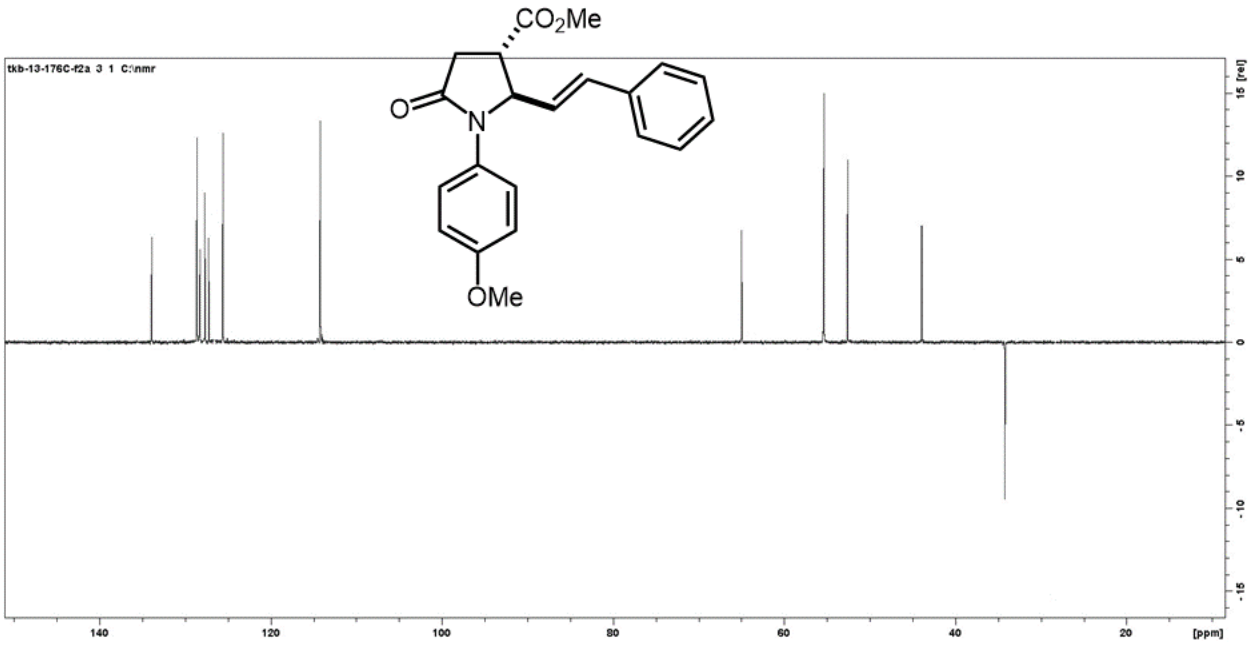


Compound 3z4

Prepared in 1.0 mmol scale using **General Procedure A**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 50:50). Amorphous solid. Yield = 144.1 mg, 41%, 95:5 dr (*trans:cis*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.26 (m, 6H), 7.30 – 7.16 (m, 1H), 6.92 – 6.82 (m, 2H), 6.57 (d, *J* = 15.9 Hz, 1H), 6.07 (dd, *J* = 15.8, 8.1 Hz, 1H), 5.00 (dd, *J* = 8.0, 5.6 Hz, 1H), 3.84 – 3.73 (m, 6H), 3.15 (ddd, *J* = 9.1, 7.6, 5.6 Hz, 1H), 3.02 – 2.83 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.52, 172.67, 171.55, 159.52, 157.66, 135.66, 133.94, 130.17, 128.65, 128.31, 127.72, 127.29, 126.65, 125.61, 114.53, 114.23, 65.02, 55.50, 55.39, 52.61, 43.96, 34.25, 28.38. **HRMS-EI$^+$** (*m/z*): calc for $C_{21}H_{21}NO_4$ $[M]^+$ 351.1471, found 351.1477.



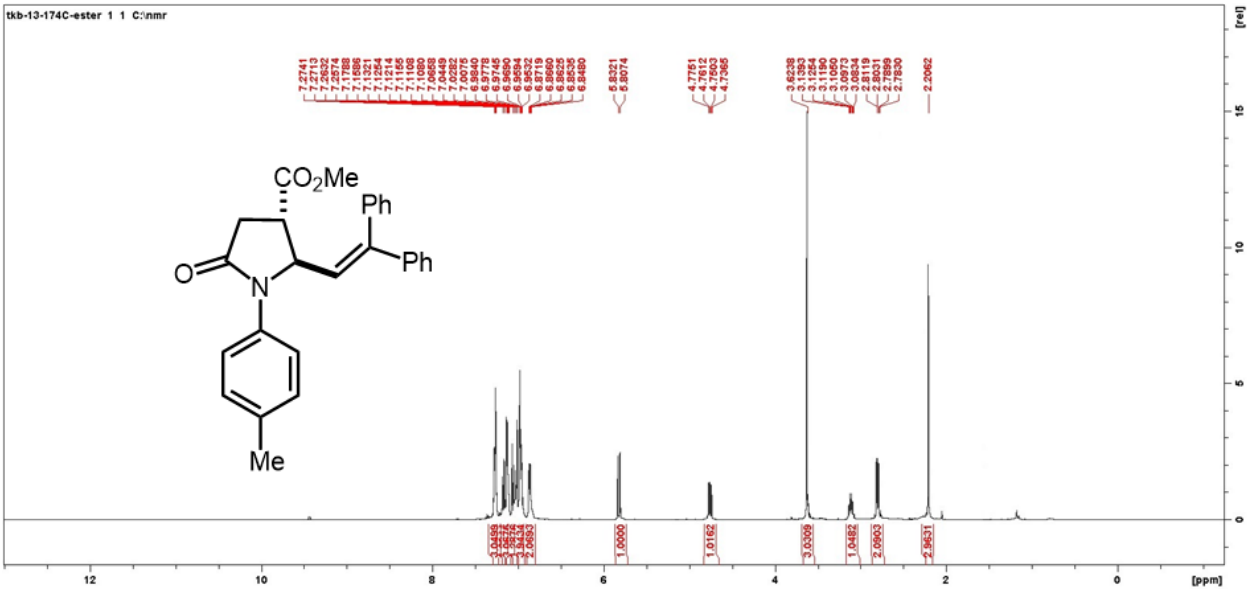


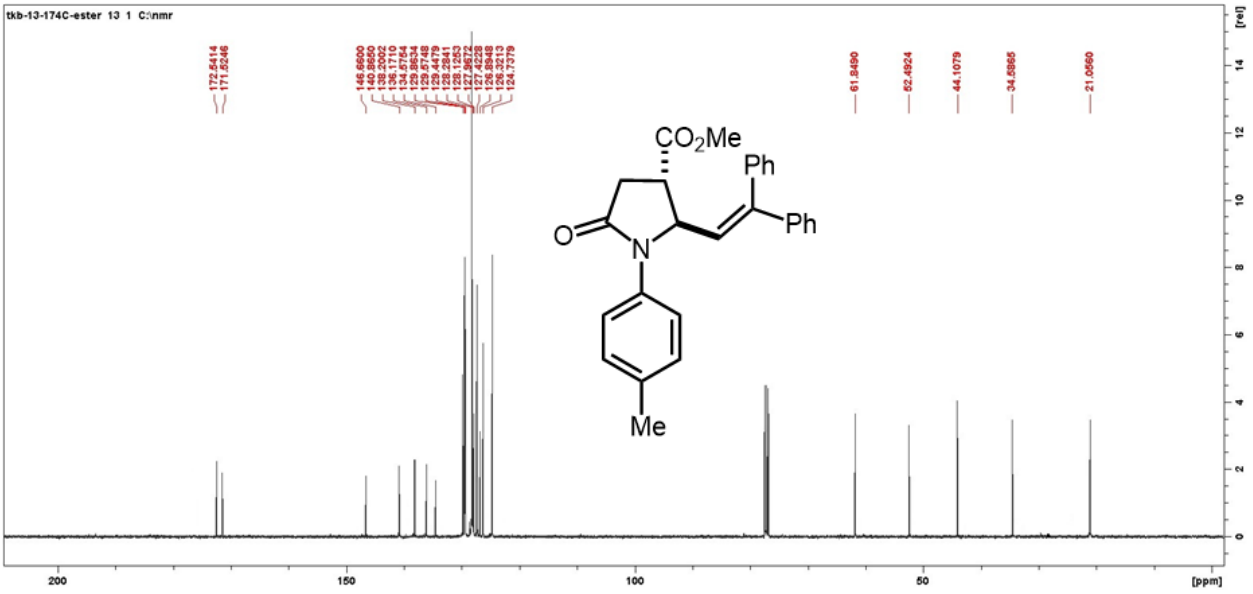


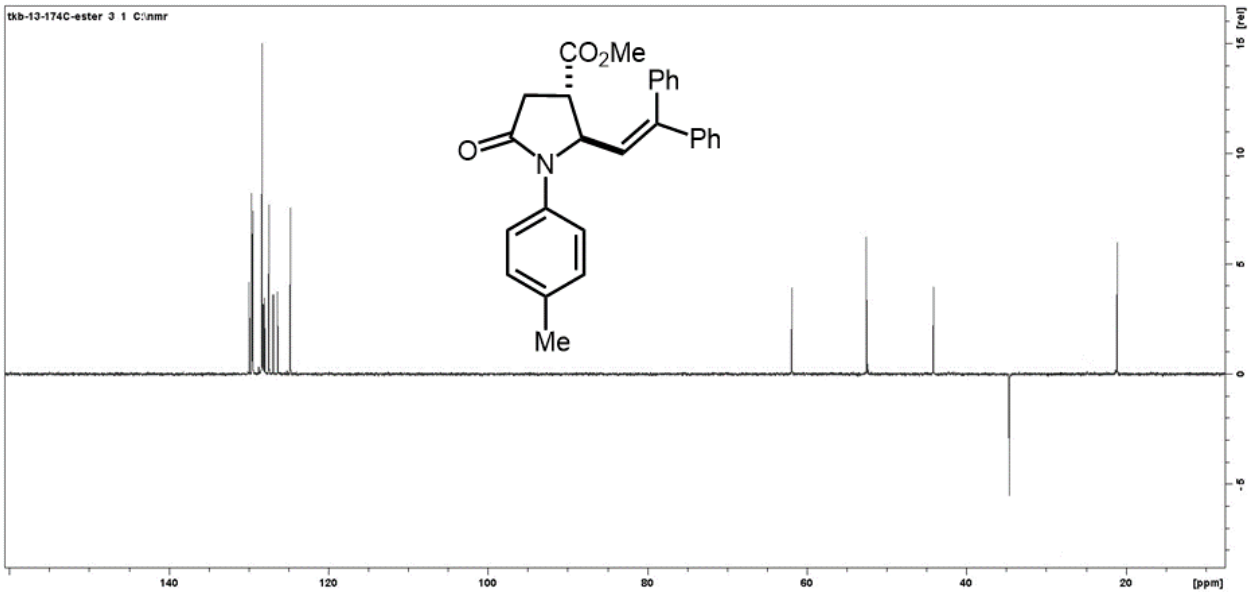
Compound 3z5

Prepared in 1.0 mmol scale using **General Procedure A**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 50:50). Amorphous solid. Yield = 189.8 mg, 43%, 95:5 dr (*trans:cis*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.22 (m, 3H), 7.18 – 7.08 (m, 9H), 6.91 – 6.80 (m, 2H), 5.80 (dd, J = 13.5, 10.2 Hz, 1H), 4.84 – 4.71 (m, 1H), 3.62 (s, 3H), 3.16 – 3.05 (m, 1H), 2.89 – 2.72 (m, 2H), 2.21 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.55, 171.53, 146.66,

140.87, 138.20, 136.17, 134.58, 129.87, 129.58, 129.45, 128.29, 127.43, 126.33, 124.74, 61.85, 52.50, 44.11, 34.59, 21.06. **HRMS-EI**$^+$ (*m/z*): calc for $C_{27}H_{25}NO_3$ $[M]^+$ 411.1834, found 411.1838.



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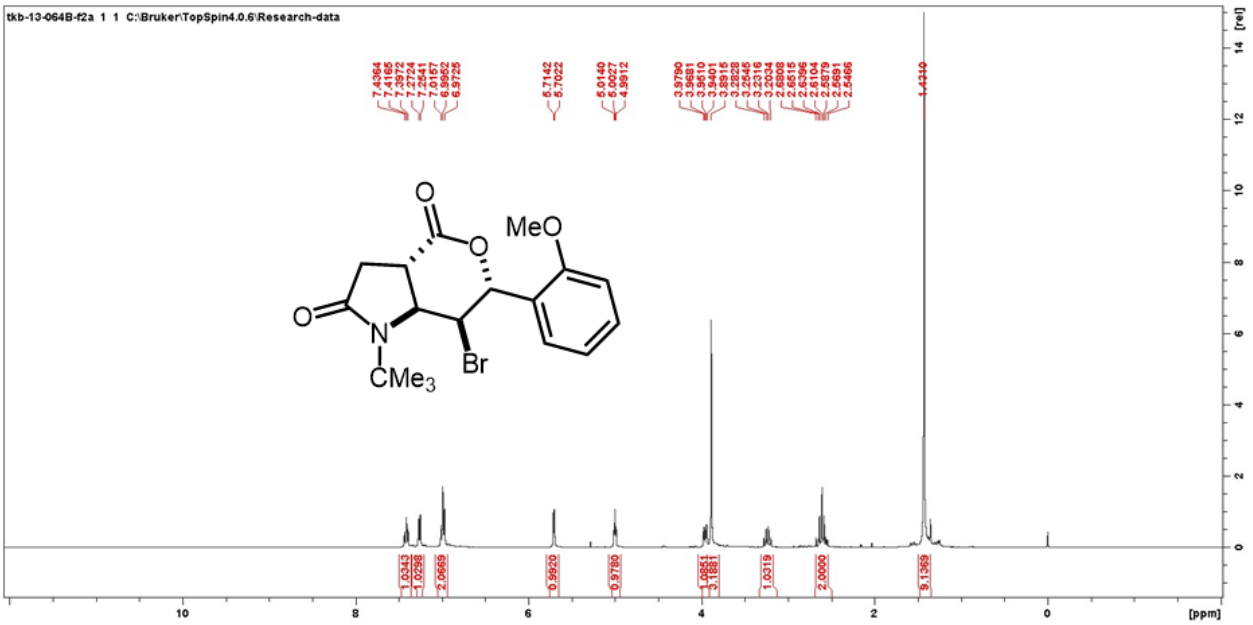
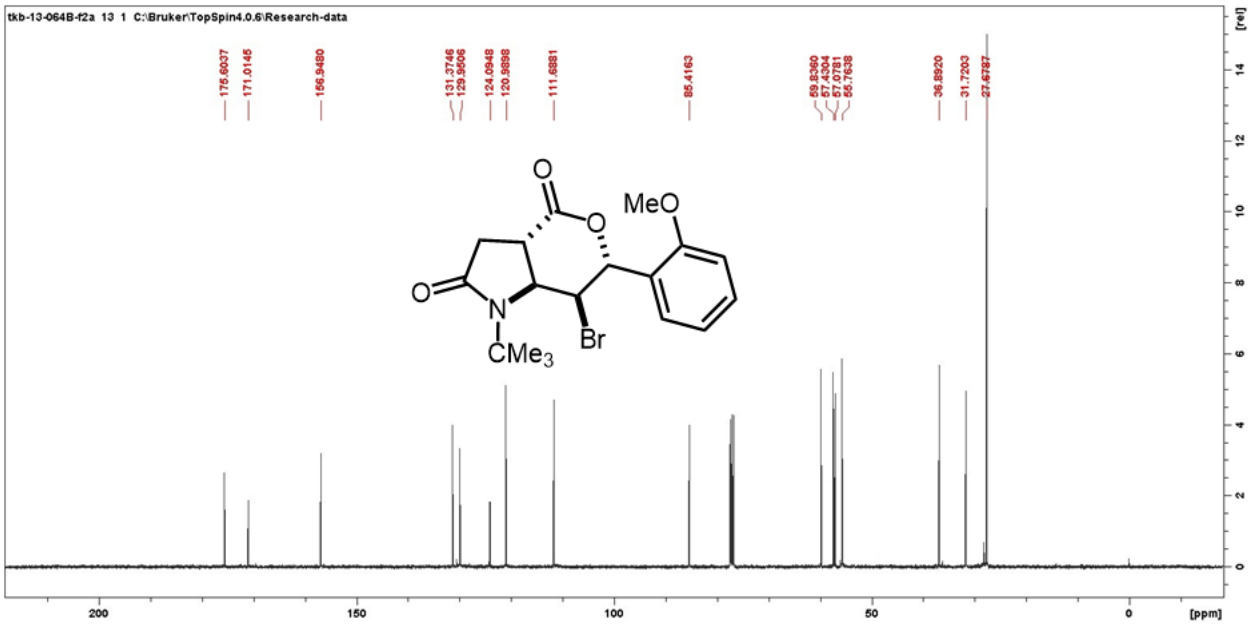
Ph
Ph
O
N
Me
140
120
100
80
60
40
20
[ppm]

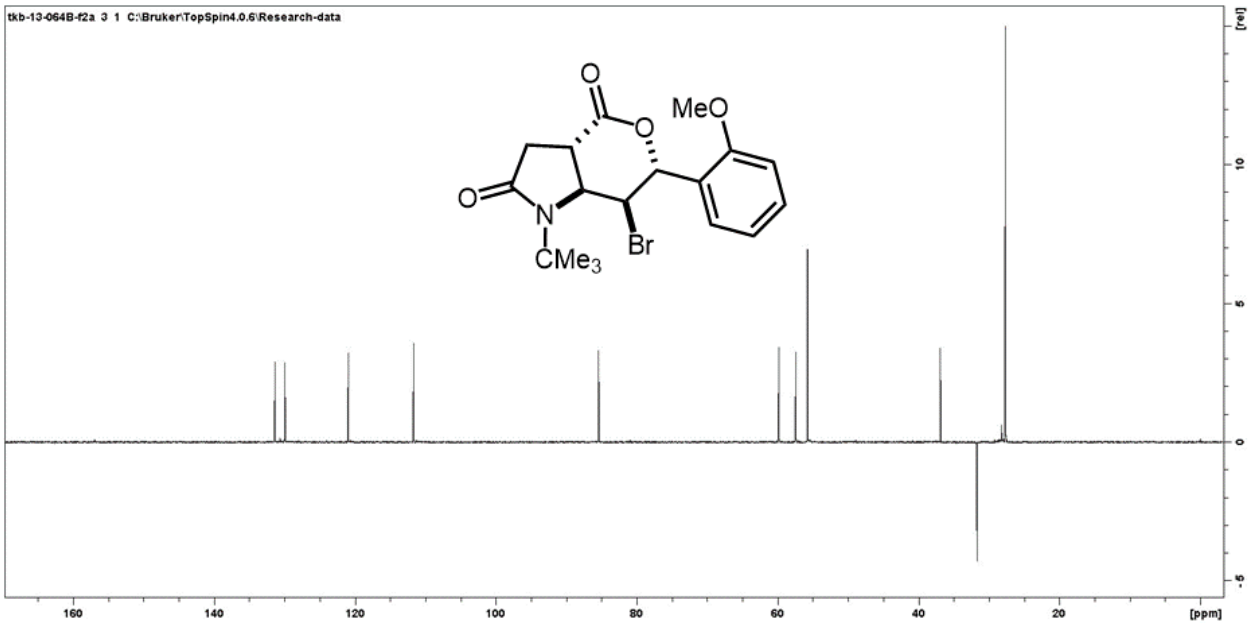
Scheme 2 Results

Compound 5a

Prepared in 1.0 mmol scale using **General Procedure B**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 50:50). Yellowish oil. Yield = 332.9 mg, 84%, 95:5 dr (*anti:syn*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (td, *J* = 7.9, 1.6 Hz, 1H), 7.31 – 7.17 (m, 1H), 7.04 – 6.89 (m, 2H), 5.71 (d, *J* = 4.9 Hz, 1H), 5.00 (t, *J* = 4.7 Hz, 1H), 3.96 (dd, *J* = 11.2, 4.4 Hz, 1H), 3.89 (s, 3H), 3.24 (td, *J* = 11.4, 8.9 Hz, 1H), 2.72 – 2.52 (m, 2H), 1.43 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.61, 171.02, 156.95, 131.38, 129.95, 124.10, 120.99, 111.69, 85.42, 59.84, 57.43, 57.08, 55.77, 36.90, 31.72, 27.68. **HRMS-EI^{+}** (*m/z*): calc for $C_{18}H_{22}BrNO_4$ $[M]^{+}$ 395.0732, found 395.0737.



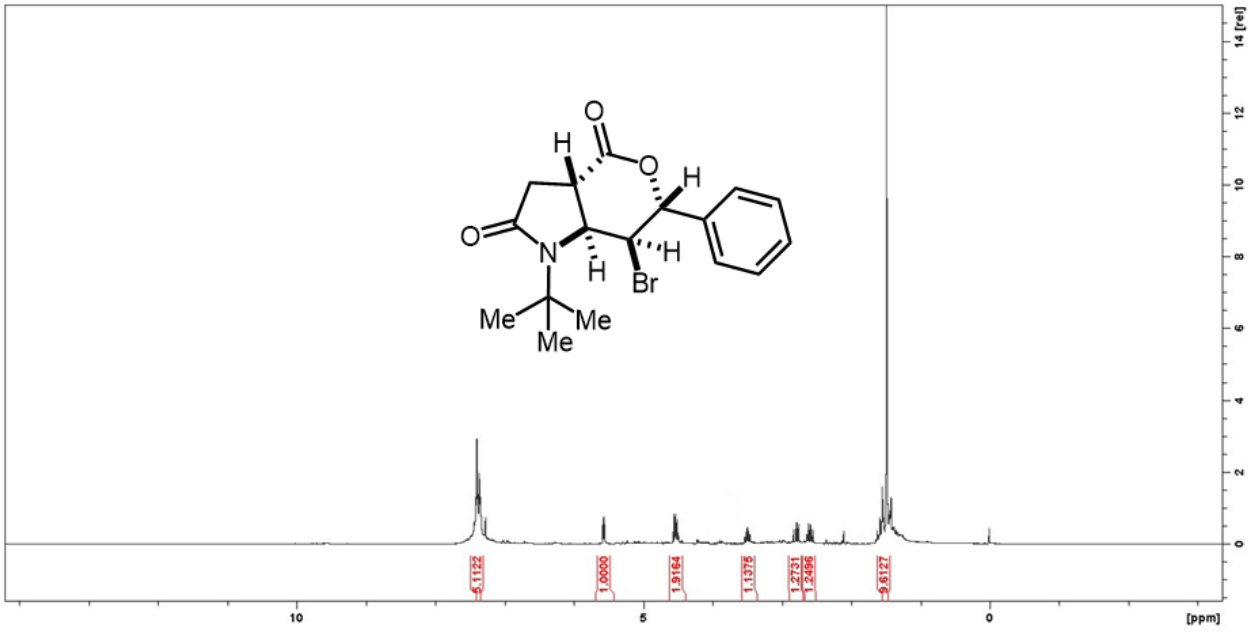


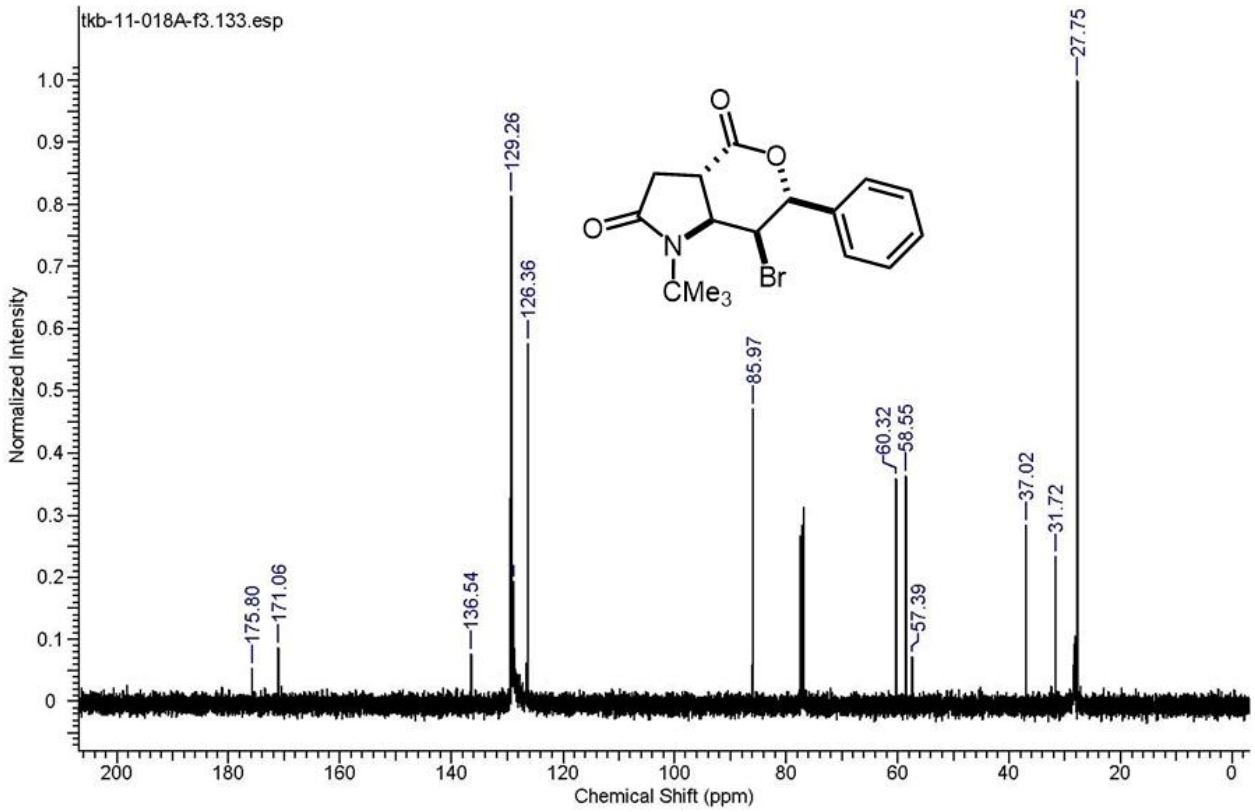


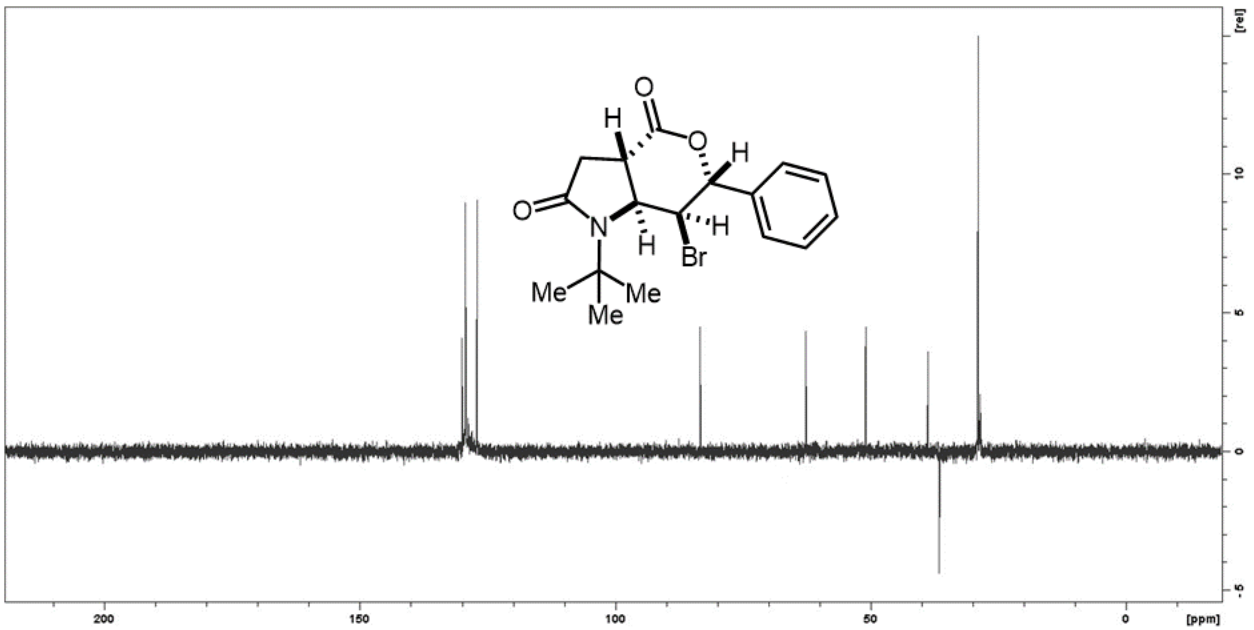
Compound 5b

Prepared in 1.0 mmol scale using **General Procedure B**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 70:30). Yellowish oil. Yield = 296.5 mg, 81%, 95:5 dr (*anti*:*syn*). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.47 – 7.37 (m, 5H), 5.63 (d, *J* = 6.0 Hz, 1H), 4.54 (dd, *J* = 6.0, 5.0 Hz, 2H), 3.74 (dd, *J* = 11.1, 5.0 Hz, 1H), 2.71 – 2.64 (m, 1H), 2.61 – 2.56 (m, 1H), 1.50 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.79, 171.06, 136.53, 129.55, 129.26,

128.87, 126.35, 85.97, 60.32, 58.55, 57.38, 37.02, 31.71, 27.75. **HRMS-EI$^+$** (*m/z*): calc for $C_{17}H_{20}BrNO_3$ $[M]^+$ 365.0627, found 365.0633.

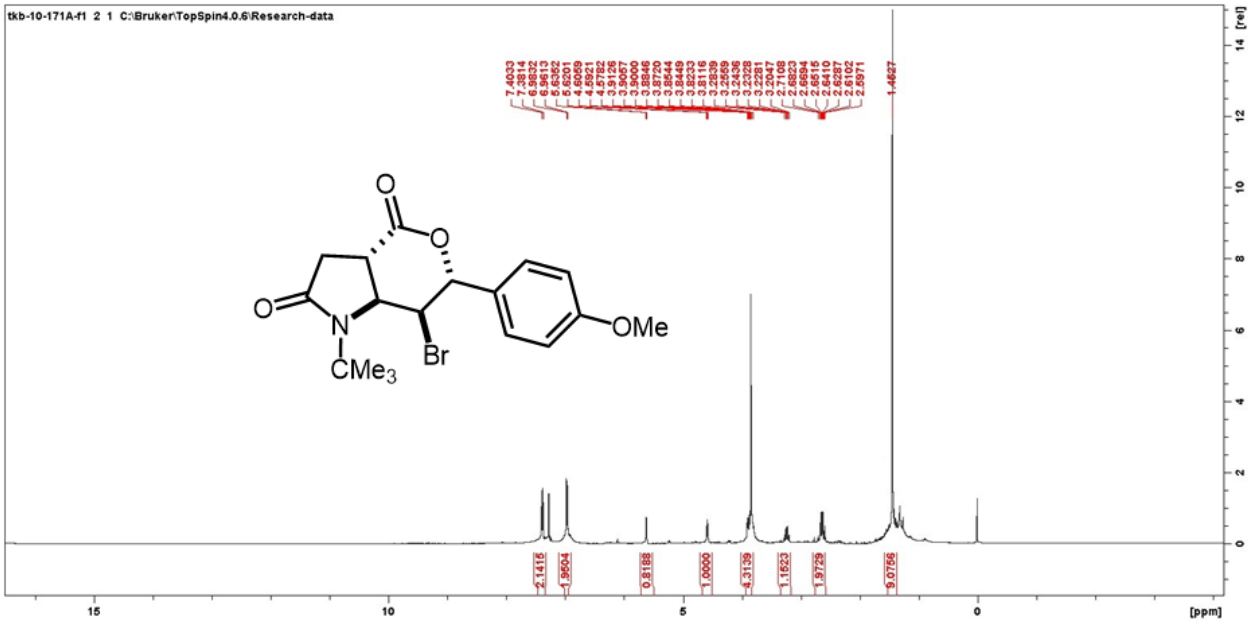


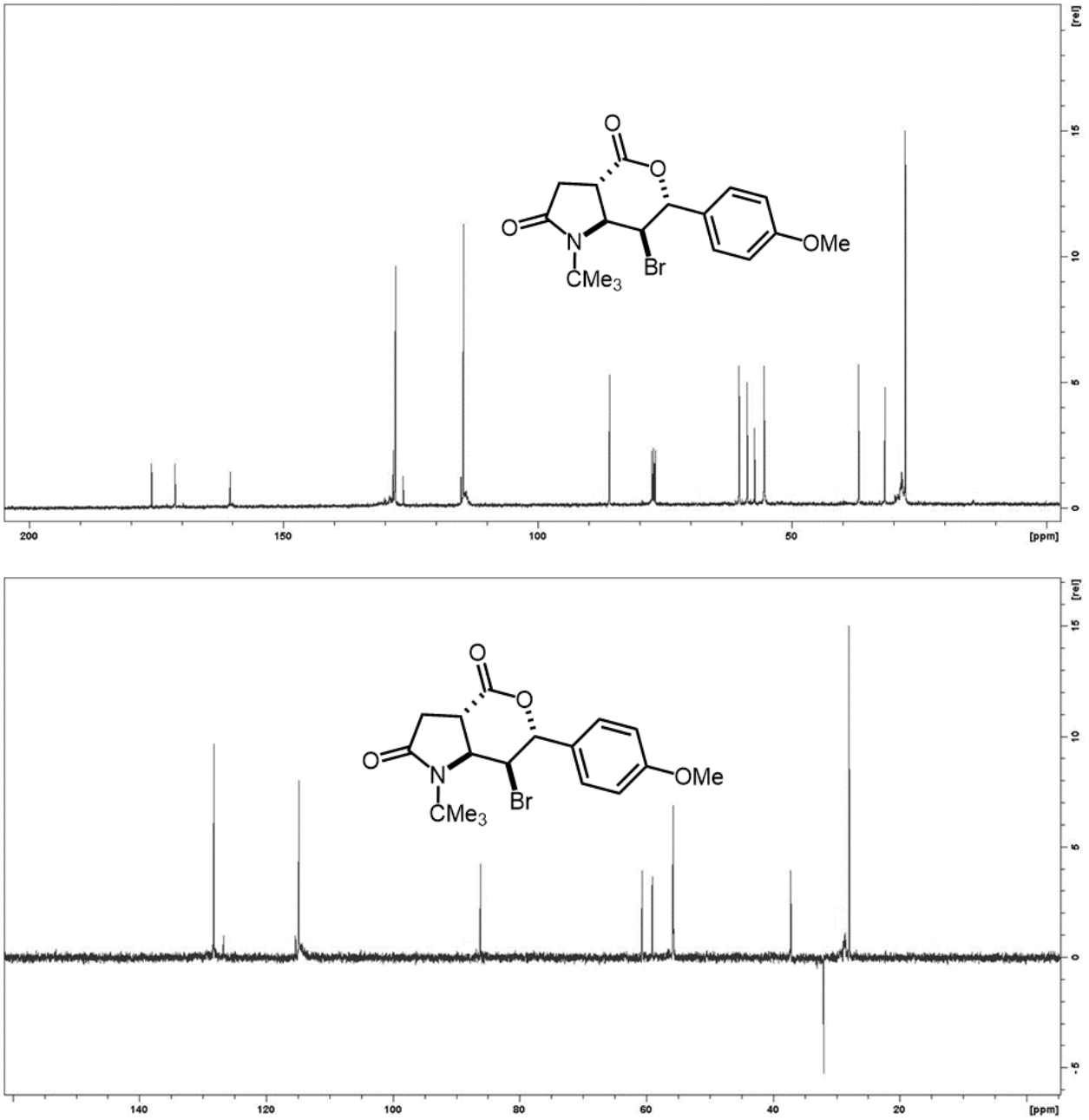




Compound 5c

Prepared in 1.0 mmol scale using **General Procedure B**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 50:50). Yellowish oil. Yield = 352.7 mg, 89%, 95:5 dr (*anti:syn*). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39 (d, *J* = 9.0 Hz 2H), 6.97 (d, *J* = 9.0 Hz, 2H), 5.63 (d, *J* = 6.1 Hz, 1H), 4.59 (dd, *J* = 6.0, 5.0 Hz, 1H), 3.94 – 3.78 (m, 4H), 3.24 (td, *J* = 11.3, 9.2 Hz, 1H), 2.73 – 2.57 (m, 2H), 1.45 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.23, 160.41, 127.94, 126.39, 114.51, 85.83, 60.34, 58.76, 57.30, 55.45, 36.87, 31.68, 27.68. **HRMS-EI^{+}** (*m/z*): calc for $C_{18}H_{22}BrNO_4$ $[M]^{+}$ 395.0732, found 395.0737.

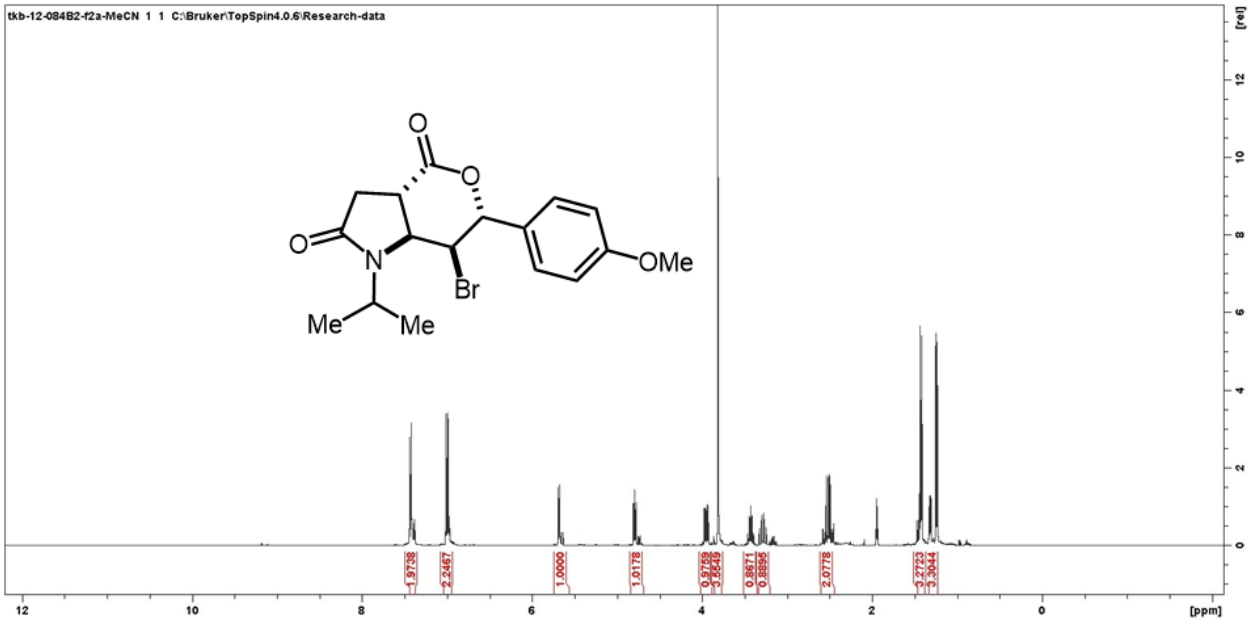


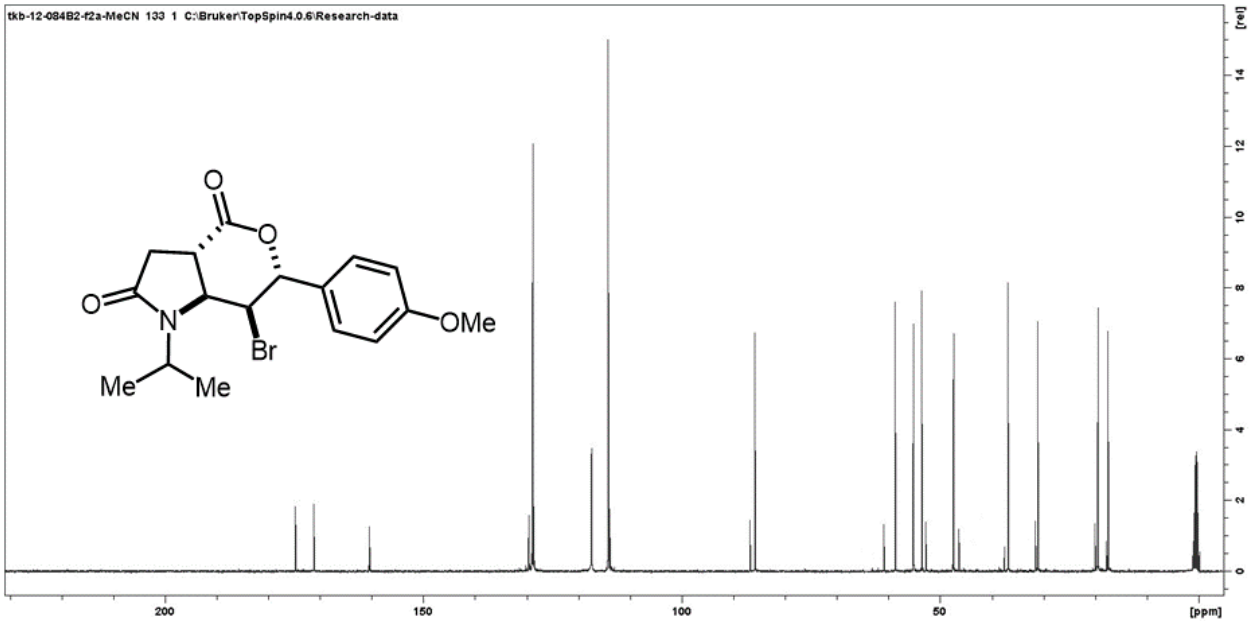


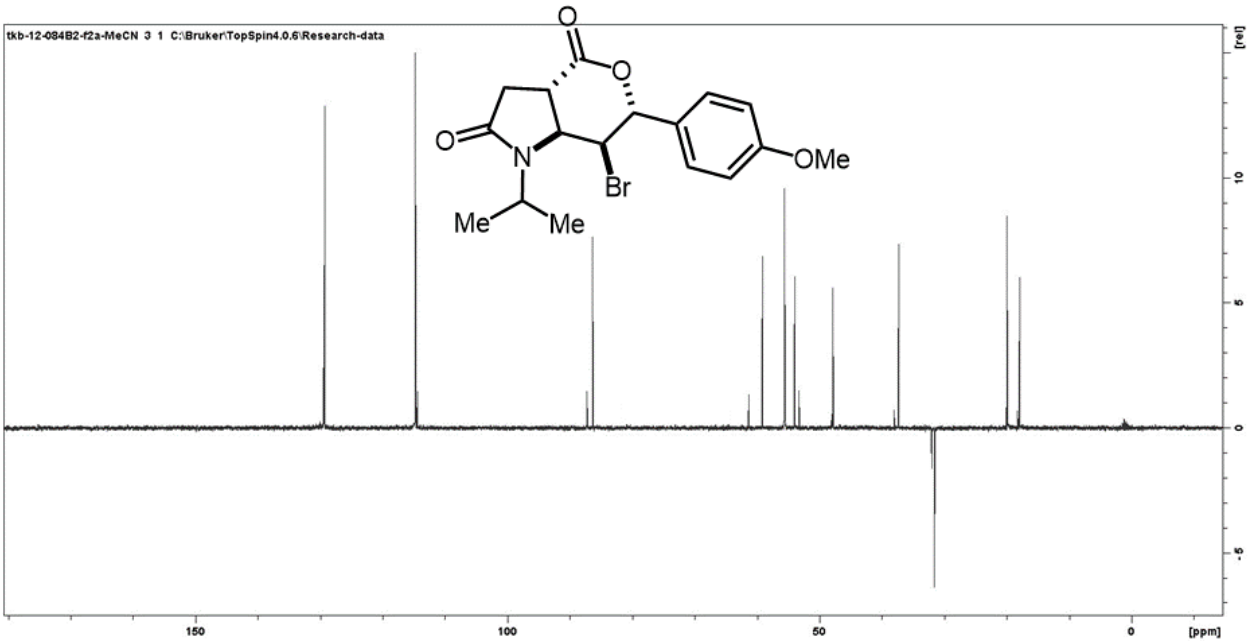
Compound 5d

Prepared in 1.0 mmol scale using **General Procedure B**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 50:50). Yellowish oil. Yield = 294.3 mg, 77%, 80:20 dr (*anti:syn*). ^{1}H NMR (400 MHz, CD_3CN) δ 7.33 (d, 2H), 6.98 (d, 2H), 5.66 (d, J = 7.1 Hz, 1H), 4.67 (dd, 1H), 3.95 (dd, J = 11.7, 5.4 Hz, 1H), 3.79 (s, 3H), 3.47 (hept, J = 6.8 Hz, 1H), 3.38 – 3.22 (m, 1H), 2.56 – 2.42 (m, 2H), 1.41 (d, J = 6.7 Hz, 3H), 1.28 (d, J = 6.7 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.76, 171.21, 160.48, 129.65, 128.87, 117.48, 114.32, 86.83, 85.91, 60.92,

58.75, 55.22, 55.19, 53.58, 52.85, 47.45, 46.39, 37.60, 36.91, 31.62, 31.15, 20.07, 19.52, 17.54, 17.05. **HRMS-EI**$^+$ (*m/z*): calc for $C_{17}H_{20}BrNO_4$ $[M]^+$ 381.0576, found 381.0579.

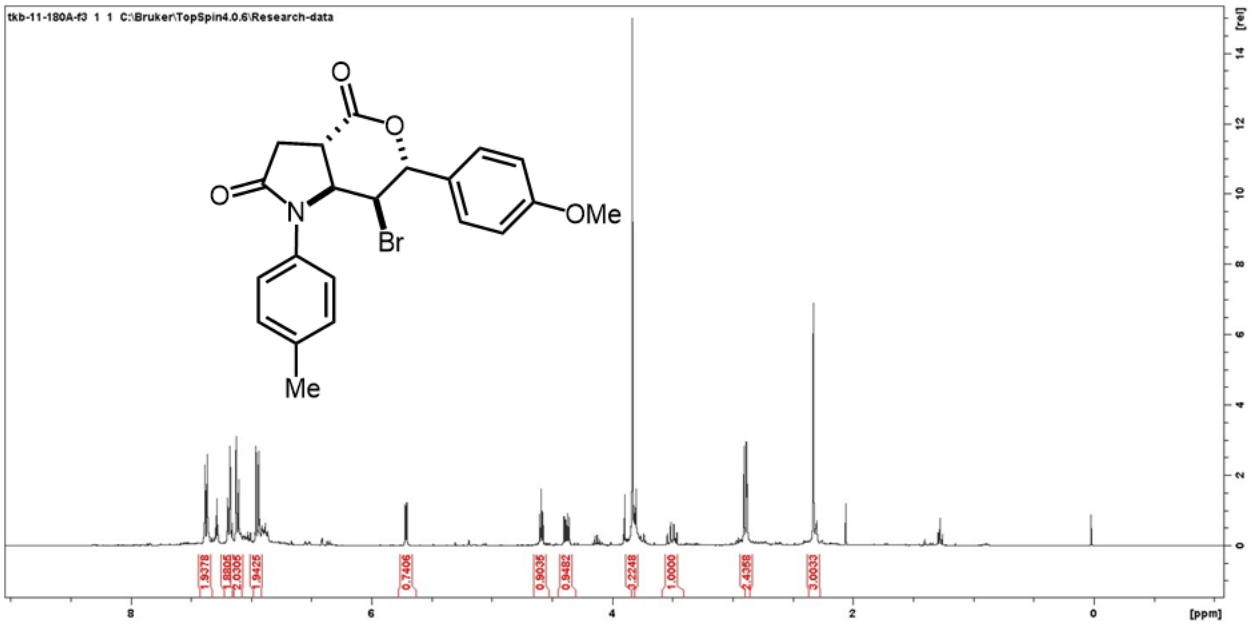






Compound 5e

Prepared in 1.0 mmol scale using **General Procedure B**. Purification: Flash chromatography on silica eluting with hexane/EtOAc (90:10 to 50:50). Yellowish oil. Yield = 365.8 mg, 85%, 95:5 dr (*anti:syn*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, *J* = 7.2 Hz, 2H), 7.22 (d, *J* = 8.5 Hz, 2H), 7.16 (d, *J* = 8.5 Hz, 2H), 6.89 (d, *J* = 7.2 Hz, 2H), 5.69 (d, *J* = 5.6 Hz, 1H), 4.57 (t, *J* = 5.4 Hz, 1H), 4.44 – 4.38 (m, 1H), 3.76 (s, 3H), 3.58 – 3.46 (m, 1H), 2.83 – 2.72 (m, 2H), 2.31 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.52, 170.17, 160.40, 136.46, 133.71, 129.98, 129.91, 128.35, 127.70, 126.39, 123.14, 114.53, 86.34, 58.62, 55.49, 51.86, 37.34, 31.16, 21.13. **HRMS-EI$^+$** (*m/z*): calc for $C_{21}H_{20}BrNO_4$ $[M]^+$ 429.0576, found 429.0572.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O
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Br
OMe
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2.4388
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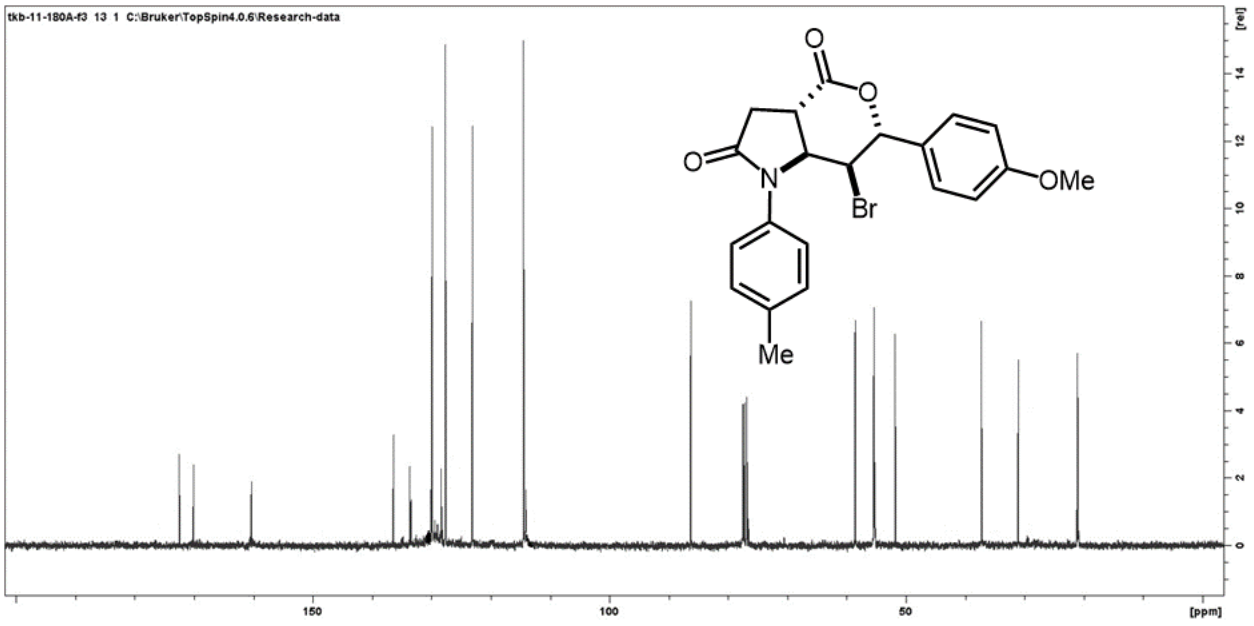
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O
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Br
OMe
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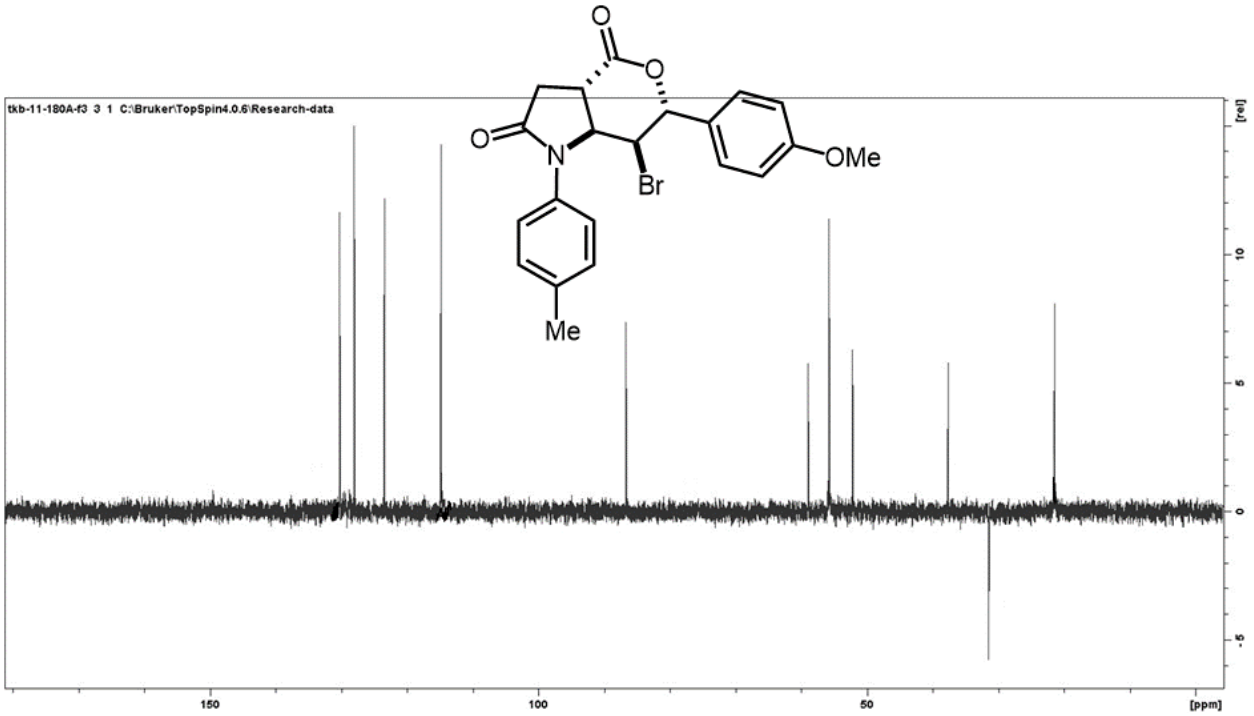
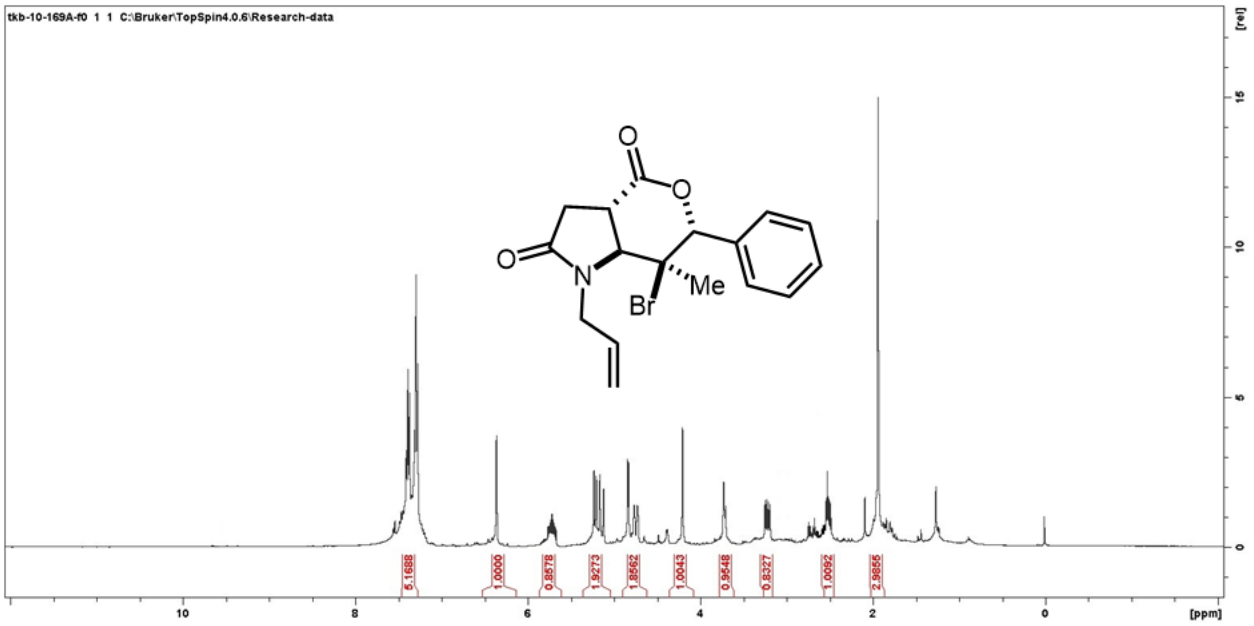


Compound 5f

Prepared in 1.0 mmol scale using **General Procedure B**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 50:50). Yellowish oil. Yield = 302.3 mg, 83%, 95:5 dr (*anti:syn*). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.59 – 7.32 (m, 5H), 6.36 (s, 1H), 5.79 (dddd, *J* = 17.4, 10.3, 7.4, 4.3 Hz, 1H), 5.30 – 5.10 (m, 2H), 4.84 (dd, *J* = 5.0, 1.3 Hz, 1H), 4.79 (ddt, *J* = 15.5, 4.0, 1.8 Hz, 1H),, 4.21 (s, 1H), 3.75 – 3.69 (m, 1H), 3.22 (dd, *J* = 15.5, 7.4 Hz, 1H), 2.51 (dt, *J* = 12.7, 5.2 Hz, 1H), 1.94 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.8, 166.6, 136.0, 132.0, 131.2, 129.0, 128.5, 127.5, 118.5, 77.9, 62.5, 46.4, 41.3, 28.2, 16.6. **HRMS-EI^{+}** (*m/z*): calc for $C_{17}H_{18}BrNO_3$ $[M]^{+}$ 363.0470, found 363.0476.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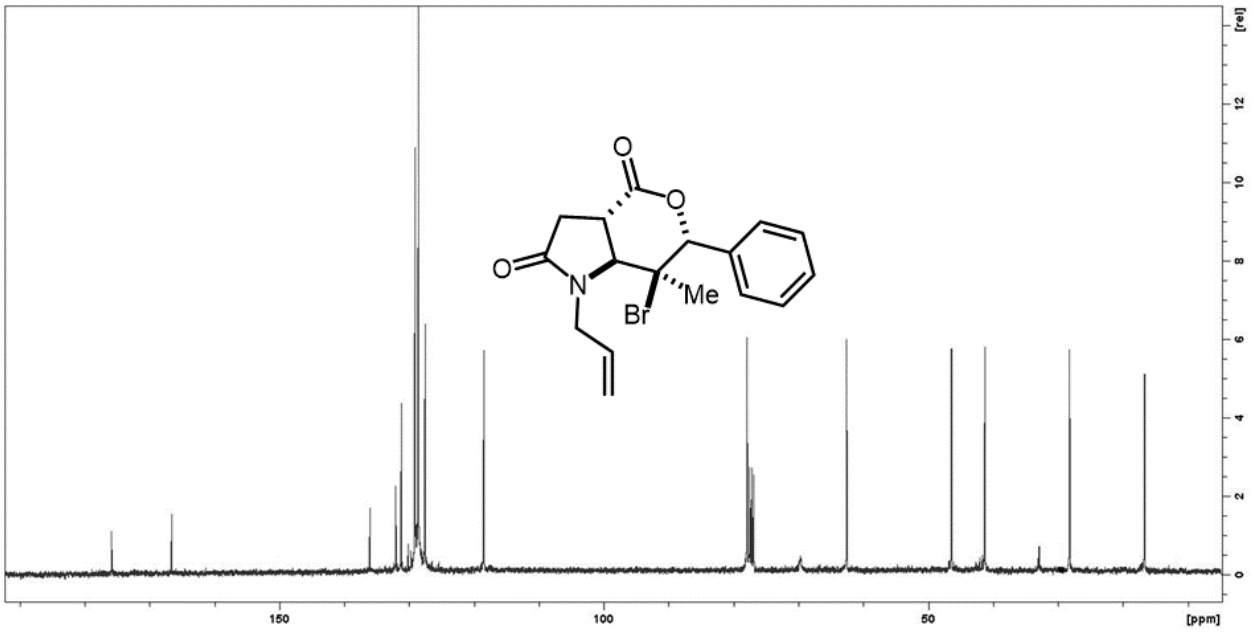
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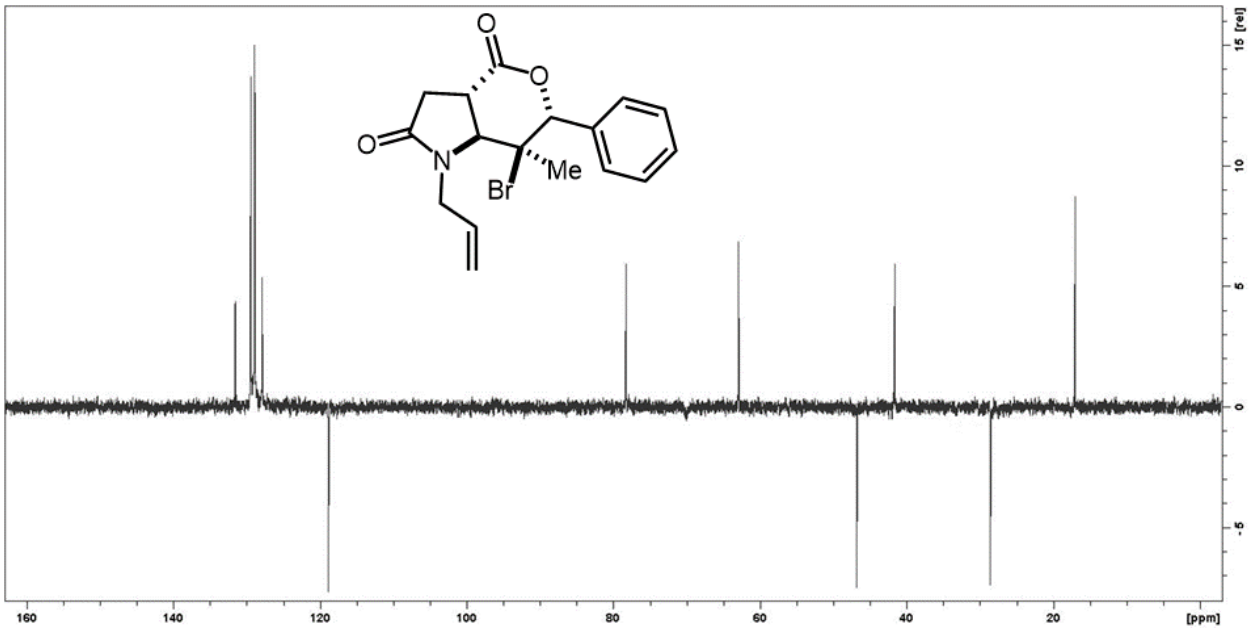
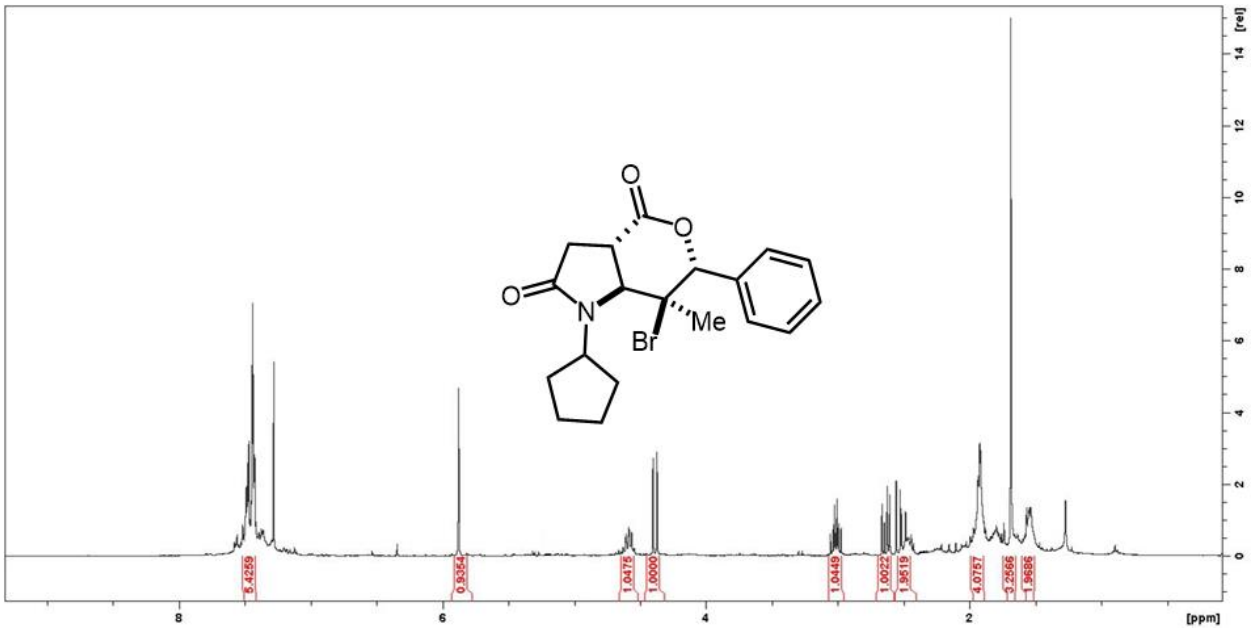
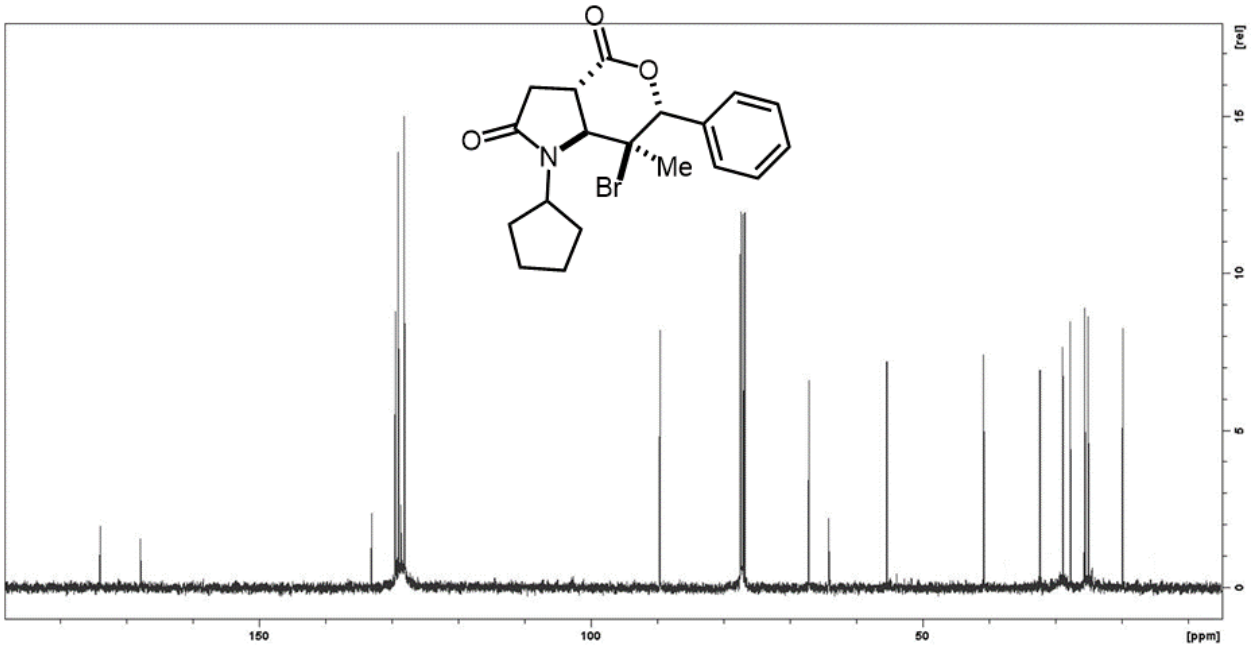
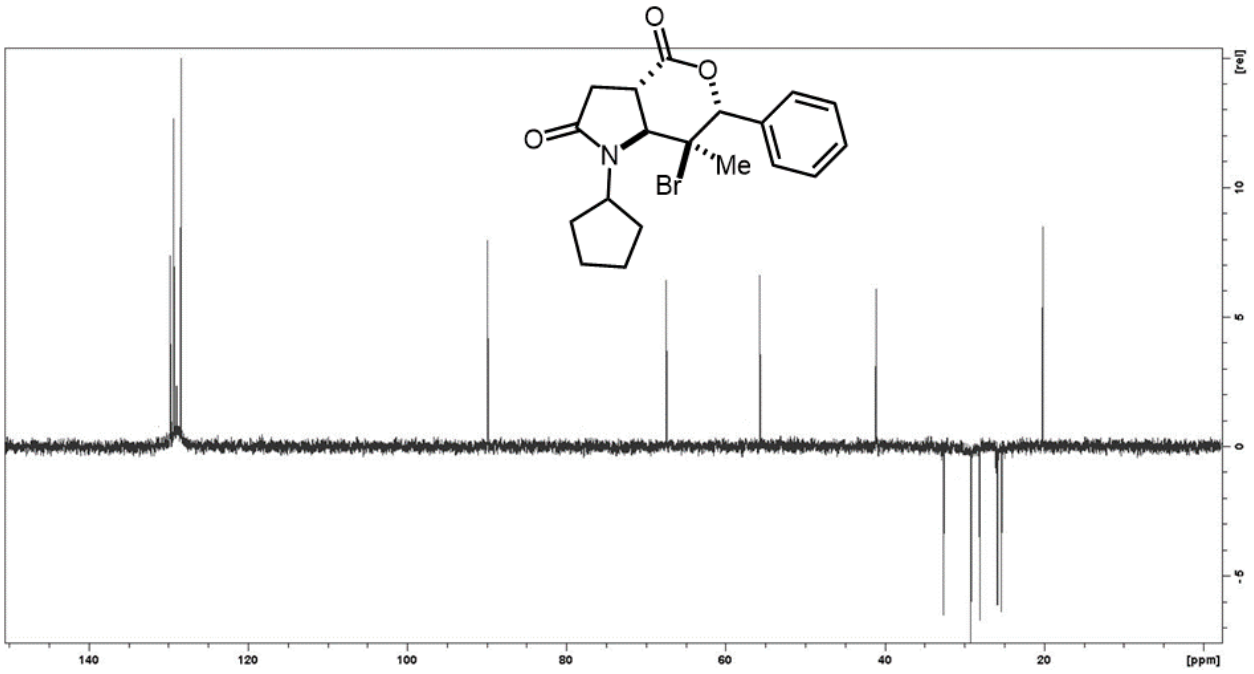


Compound 5g

Prepared in 1.0 mmol scale using **General Procedure B**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 70:30). Yellowish oil. Yield = 309.9 mg, 79%, 95:5 dr (*anti:syn*). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.62 – 7.42 (m, 5H), 5.88 (s, 1H), 4.71 – 4.52 (m, 1H), 4.39 (d, *J* = 12.2 Hz, 1H), 3.02 (td, *J* = 12.2, 7.5 Hz, 1H), 2.64 (dd, *J* = 16.2, 7.4 Hz, 1H), 2.59 – 2.39 (m, 2H), 1.97 – 1.85 (m, 4H), 1.69 (s, 3H), 1.62 – 1.49 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.9, 167.8, 133.0, 129.4, 129.0, 128.1, 89.6, 67.1, 64.2, 55.4, 40.8, 32.3, 28.9, 27.7, 25.5, 25.0, 19.9. **HRMS-EI^{+}** (*m/z*): calc for $C_{19}H_{22}BrNO_3$ $[M]^{+}$ 391.0783, found 391.0788.



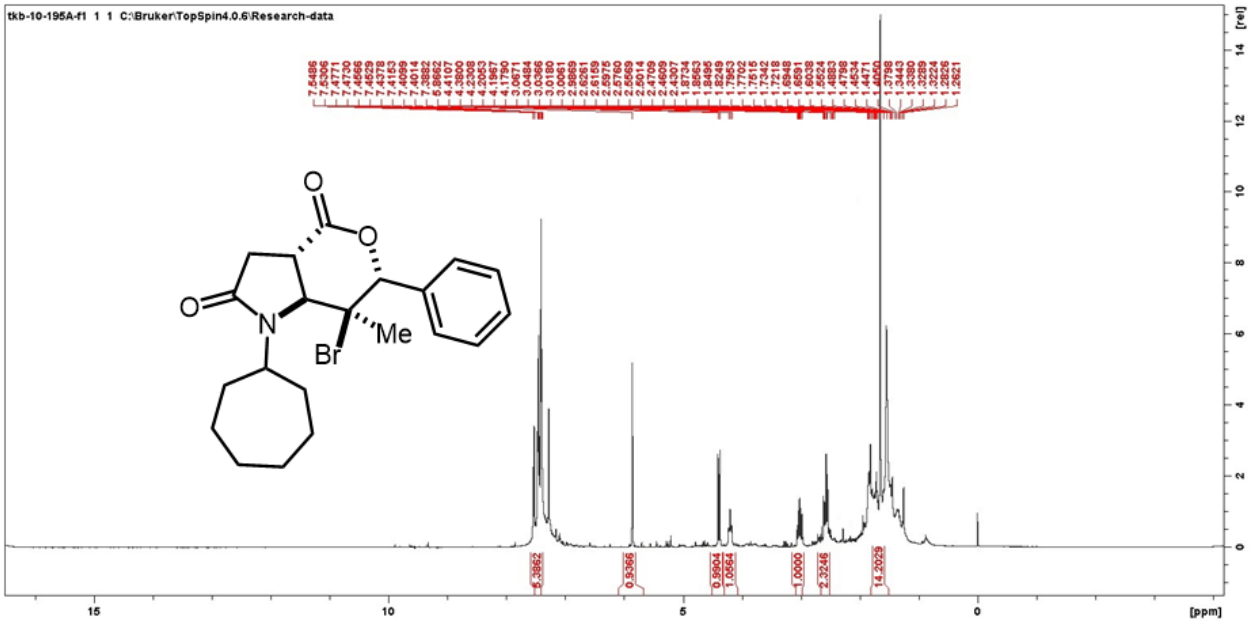


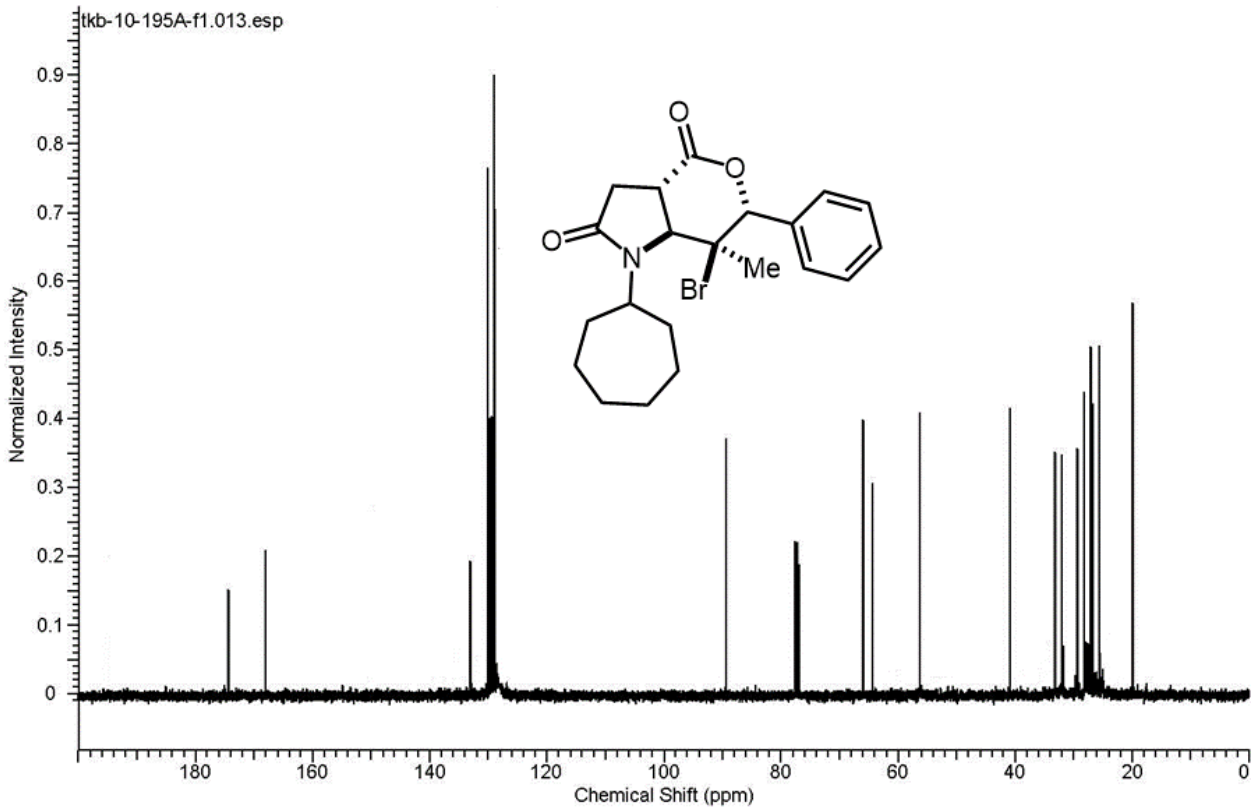


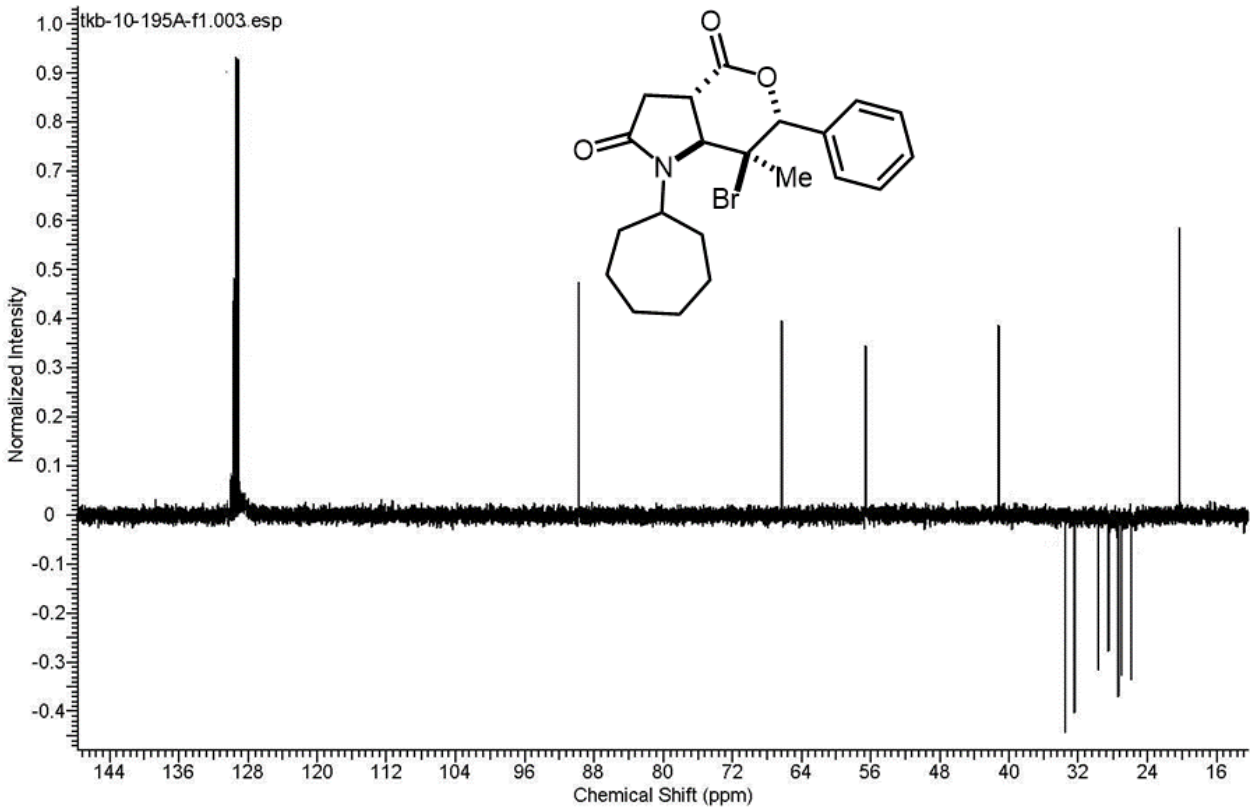
Compound 5h

Prepared in 1.0 mmol scale using **General Procedure B**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 70:30). Yellowish oil. Yield = 327.8 mg, 78%, 95:5 dr (*anti:syn*). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.54 – 7.38 (m, 5H), 5.87 (s, 1H), 4.40 (d, *J* = 12.3 Hz, 1H), 4.21 (tt, *J* = 10.6, 3.7 Hz, 1H), 3.03 (td, *J* = 12.3, 7.6 Hz, 1H), 2.62 – 2.43 (m, 2H),

1.87 – 1.26 (m, 15H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.3, 168.0, 130.1, 129.0, 128.0, 89.5, 65.9, 64.4, 56.3, 40.8, 33.2, 32.1, 29.3, 28.2, 27.1, 26.7, 25.6, 19.9. **HRMS-EI$^+$** (*m/z*): calc for $C_{21}H_{26}BrNO_3$ $[M]^+$ 419.1096, found 419.1093.

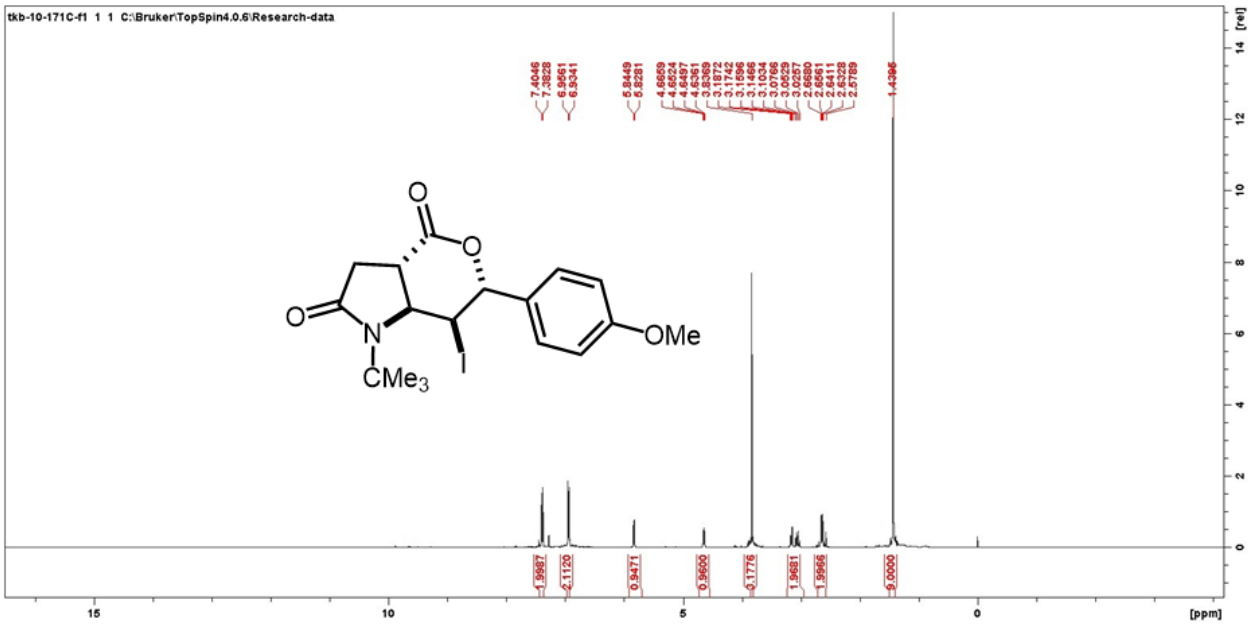






Compound 5i

Prepared in 0.50 mmol scale using **General Procedure B**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 50:50). Yellowish oil. Yield = 206.1 mg, 93%, 95:5 dr (*anti:syn*). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39 (d, *J* = 9.0 Hz 2H), 6.95 (d, *J* = 9.0 Hz, 2H), 5.84 (d, *J* = 6.7 Hz, 1H), 4.65 (dd, *J* = 6.7, 5.2 Hz, 1H), 3.85 (s, 3H), 3.17 (dd, *J* = 11.0, 5.2 Hz, 1H), 3.06 (td, *J* = 10.8, 9.2 Hz, 1H), 2.66 – 2.56 (m, 2H), 1.44 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.35, 171.59, 160.41, 130.45, 128.28, 114.51, 87.35, 60.60, 57.47, 55.46, 44.72, 38.18, 31.73, 27.95. **HRMS-EI$^+$** (*m/z*): calc for $C_{18}H_{22}INO_4$ $[M]^+$ 443.0594, found 443.0598.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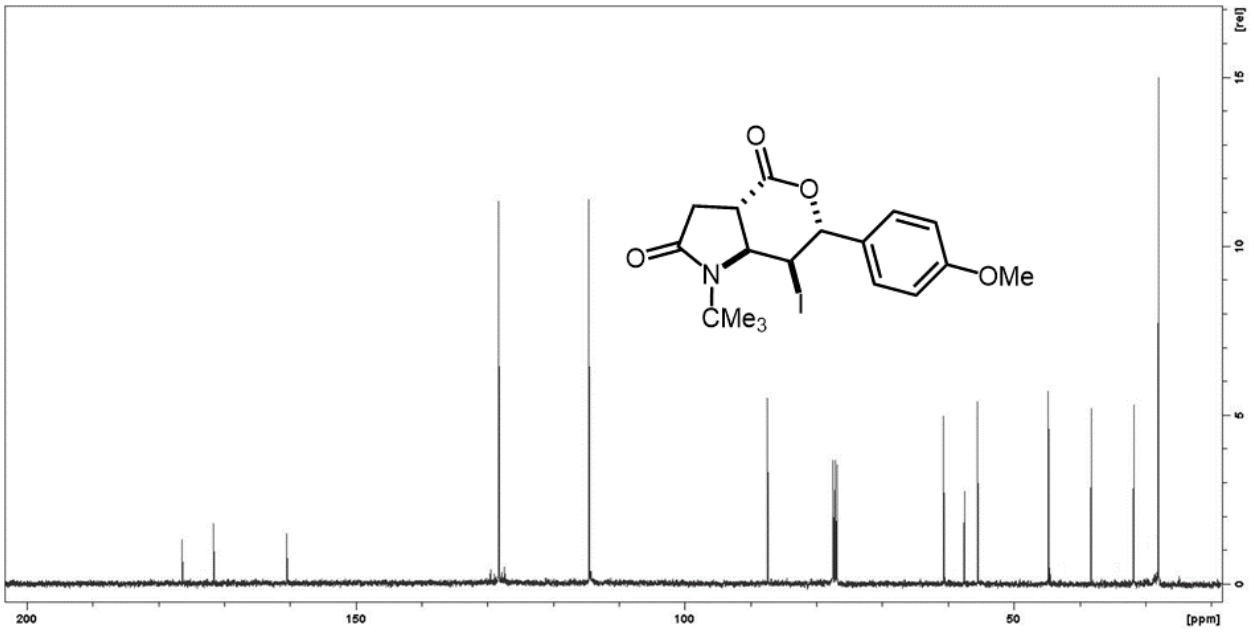
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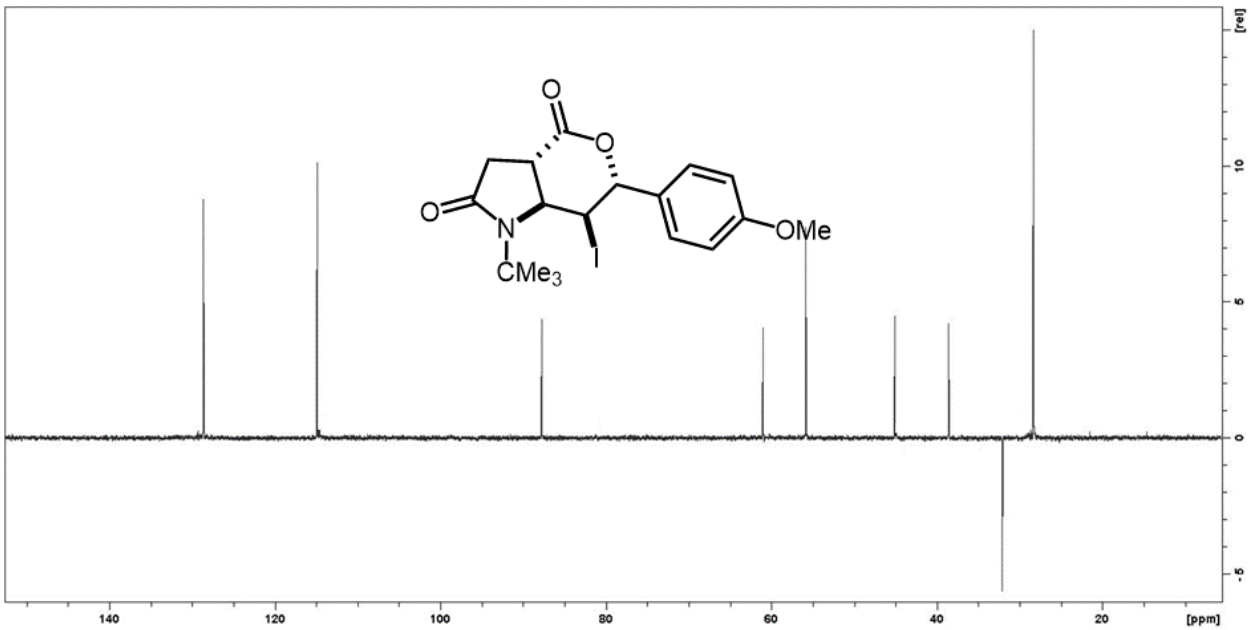
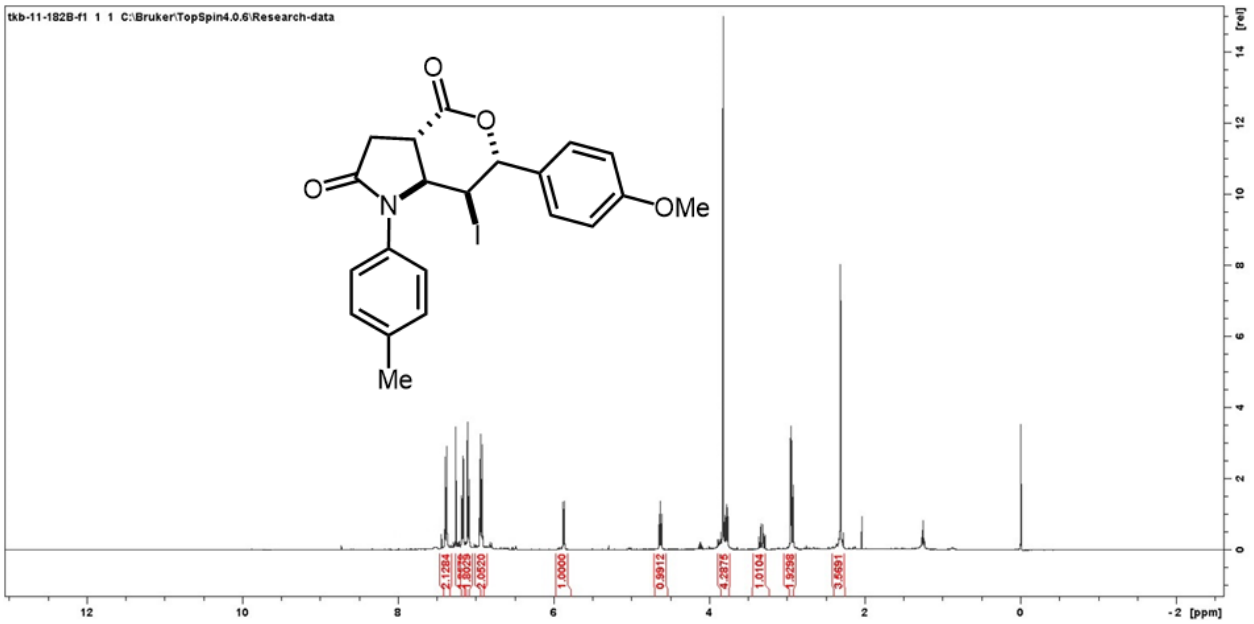


Compound 5j

Prepared in 0.50 mmol scale using **General Procedure B**. Purification: Flash chromatography on silica eluting with hexane/acetone (90:10 to 50:50). Yellowish oil. Yield = 212.4 mg, 89%, 95:5 dr (*anti:syn*). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, *J* = 7.5 Hz, 2H), 7.22 (d, *J* = 8.1 Hz, 2H), 7.16 (d, *J* = 8.1 Hz, 2H), 6.84 (d, *J* = 7.5 Hz, 2H), 5.86 (d, *J* = 6.6 Hz, 1H), 4.68 (dd, *J* = 6.6, 5.8 Hz, 1H), 3.81 (s, 3H), 3.80 – 3.69 (m, 1H), 3.37 (td, *J* = 11.0, 9.2 Hz, 1H), 2.98 (dd, *J* = 11.6, 2.4 Hz, 2H), 2.30 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.49, 170.50, 160.46, 136.28, 133.81, 129.99, 129.86, 128.20, 128.09, 126.37, 123.05, 114.52, 87.72, 58.44, 55.49, 38.72, 34.06, 31.11, 28.51, 21.11. **HRMS-EI^{+}** (*m/z*): calc for $C_{21}H_{20}INO_4$ $[M]^{+}$ 477.0437, found 477.0443.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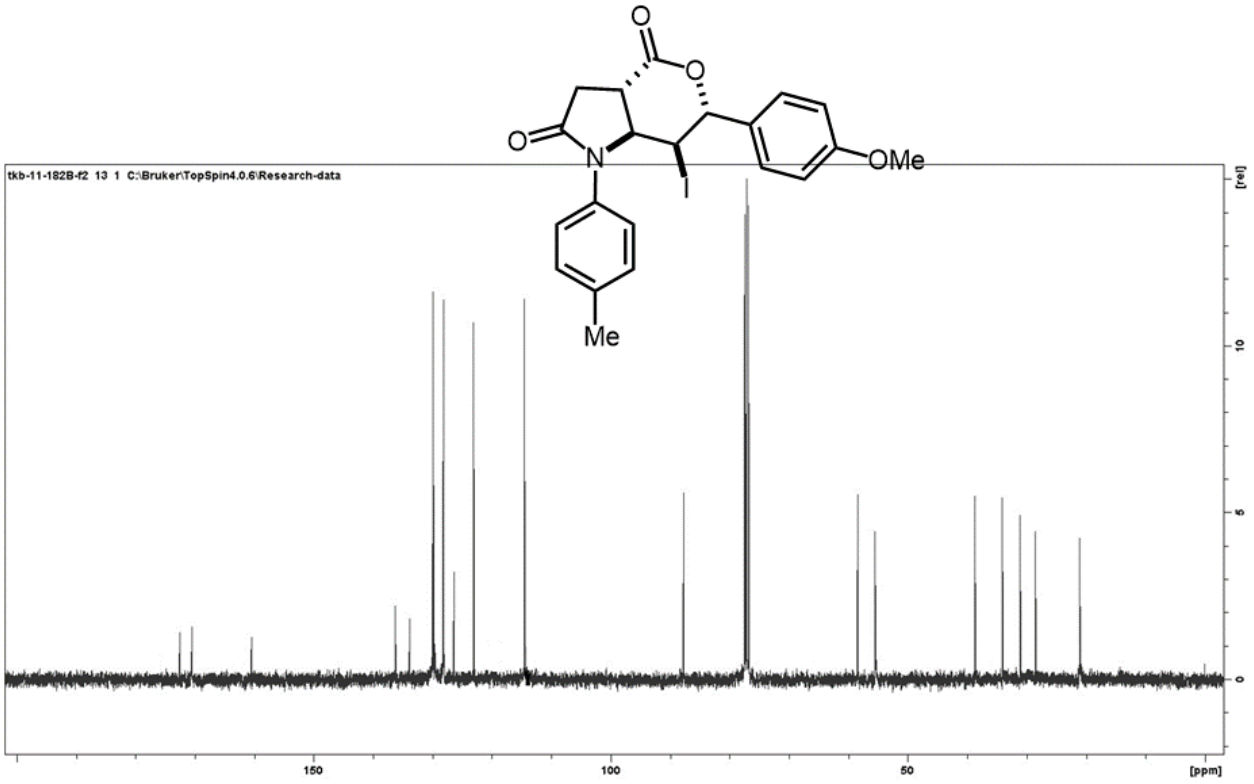
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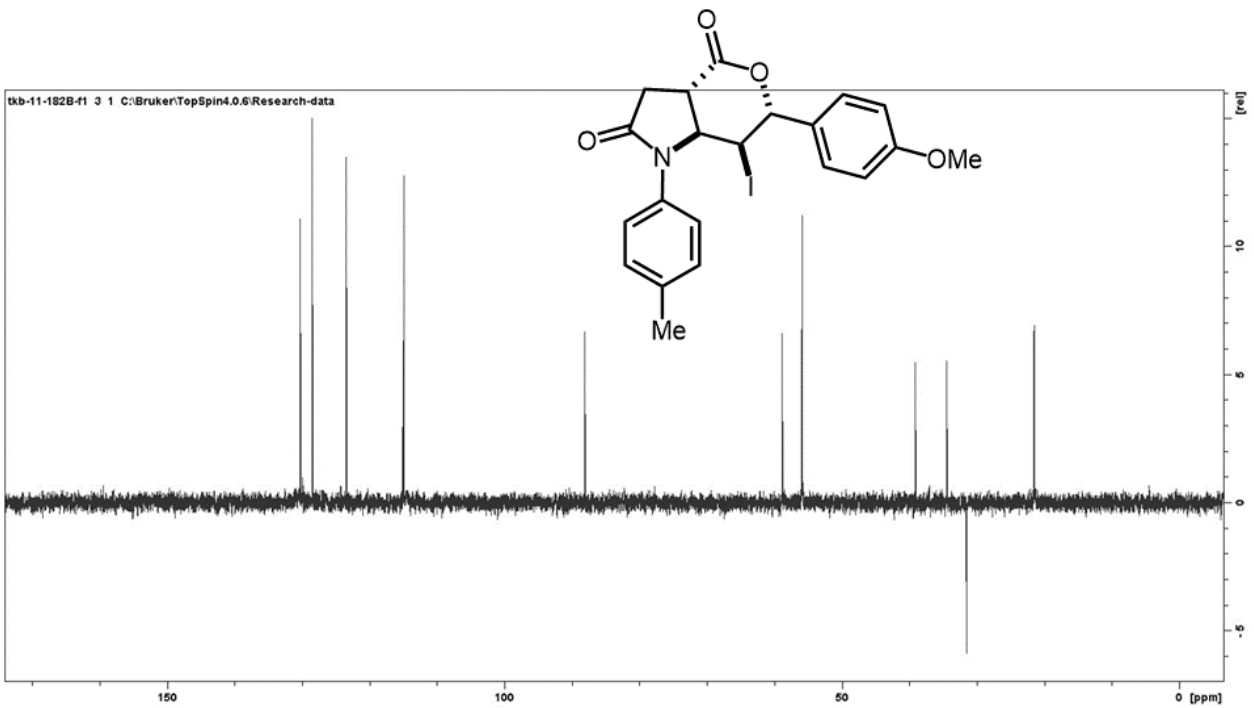
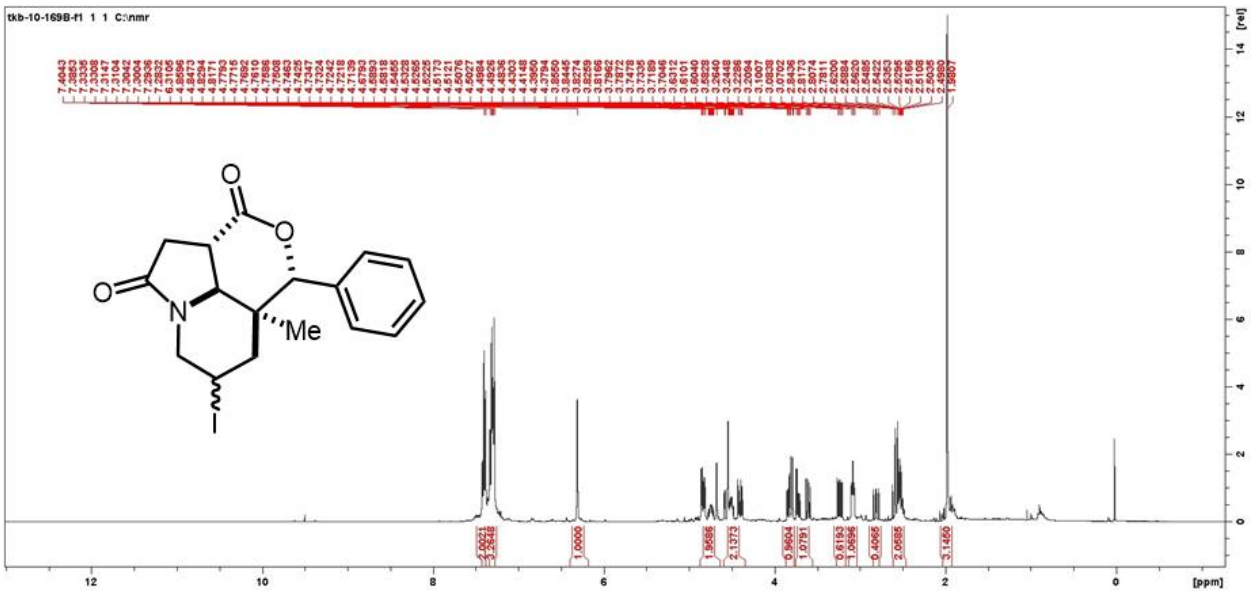


Compound 6

Prepared in 1.0 mmol scale using **General Procedure B**. Purification: Flash chromatography on silica eluting with hexane/acetone (95:5 to 70:30). Yellowish oil. Yield = 361.9 mg, 88%, 50:50 dr. ^{1}H NMR (400 MHz, Chloroform-*d, mixture of diastereomers*) δ 7.45 – 7.28 (m, 5H), 6.31 (s, 1H), 4.95 – 4.79 (m, 2H), 4.64 – 4.45 (m, 2H), 3.88 – 3.77 (m, 2H), 3.24 (dd, *J* = 14.2, 7.7 Hz, 0.6H), 3.09 (tt, *J* = 6.7, 1.6 Hz, 1H), 2.81 (dd, *J* = 14.5, 10.6 Hz, 0.4H), 2.66 – 2.45 (m, 2H), 1.98 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$, mixture of diastereomers) δ 175.38, 175.01, 167.61, 167.42, 135.82, 135.71, 132.14, 131.87, 129.09, 129.08, 129.03, 128.99, 128.68, 128.56, 128.51, 127.71, 127.68, 65.87, 64.56, 51.90, 48.77, 47.52, 46.00, 41.15, 40.94, 35.38, 34.12, 29.77, 28.06, 28.03, 16.92, 16.71. **HRMS-EI^{+}** (*m/z*): calc for $C_{17}H_{18}INO_3$ $[M]^{+}$ 411.0331, found 411.0337.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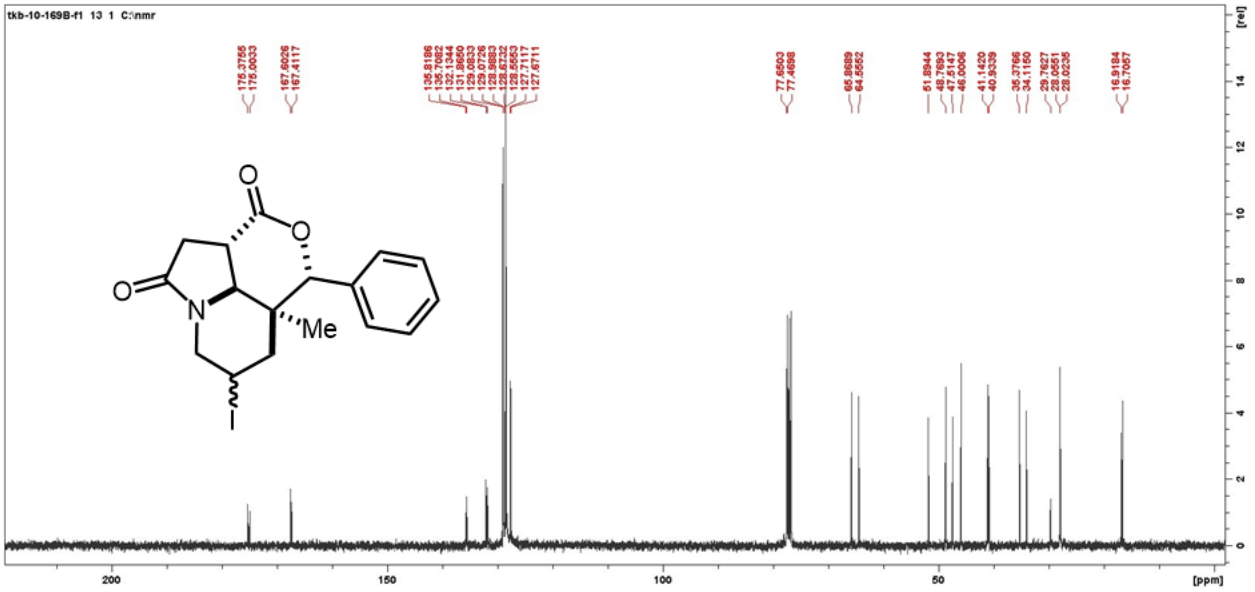
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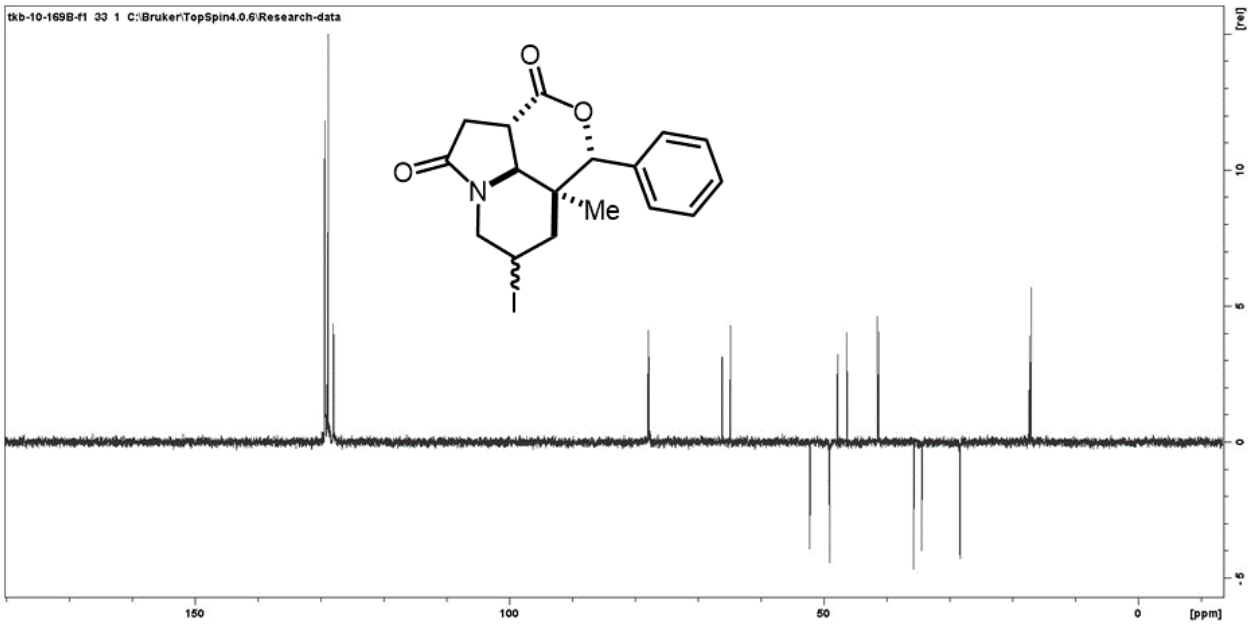
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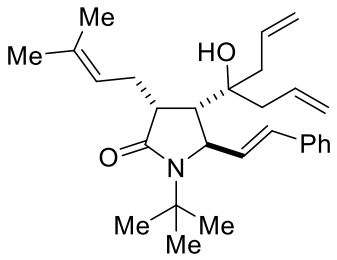
0
[ppm]

Scheme 3 results

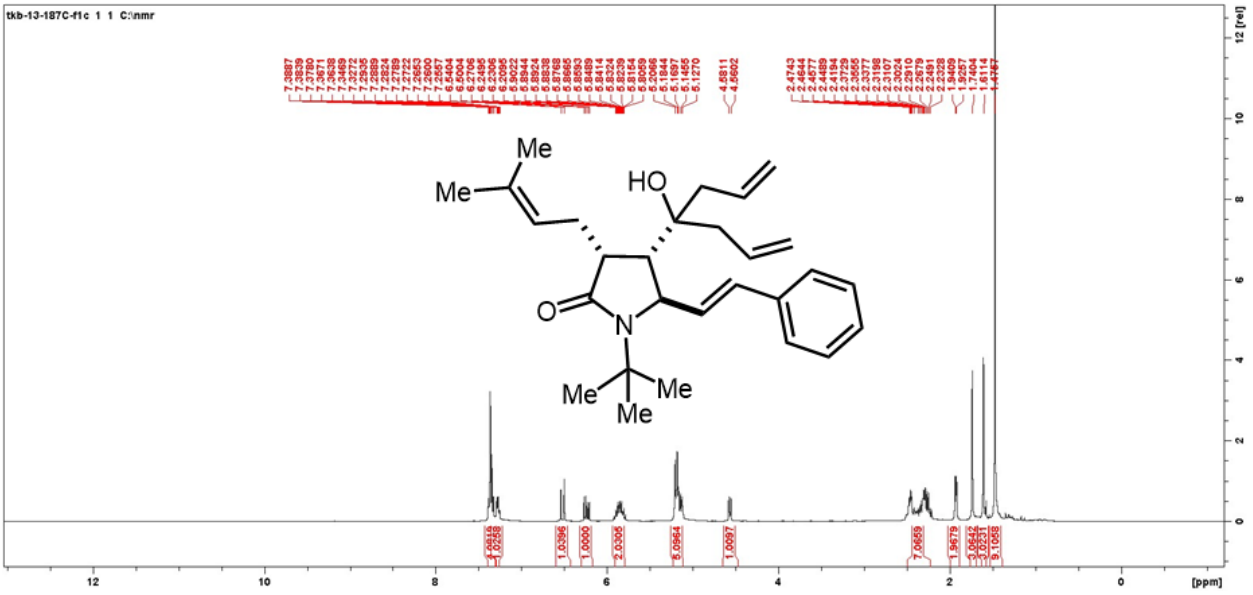


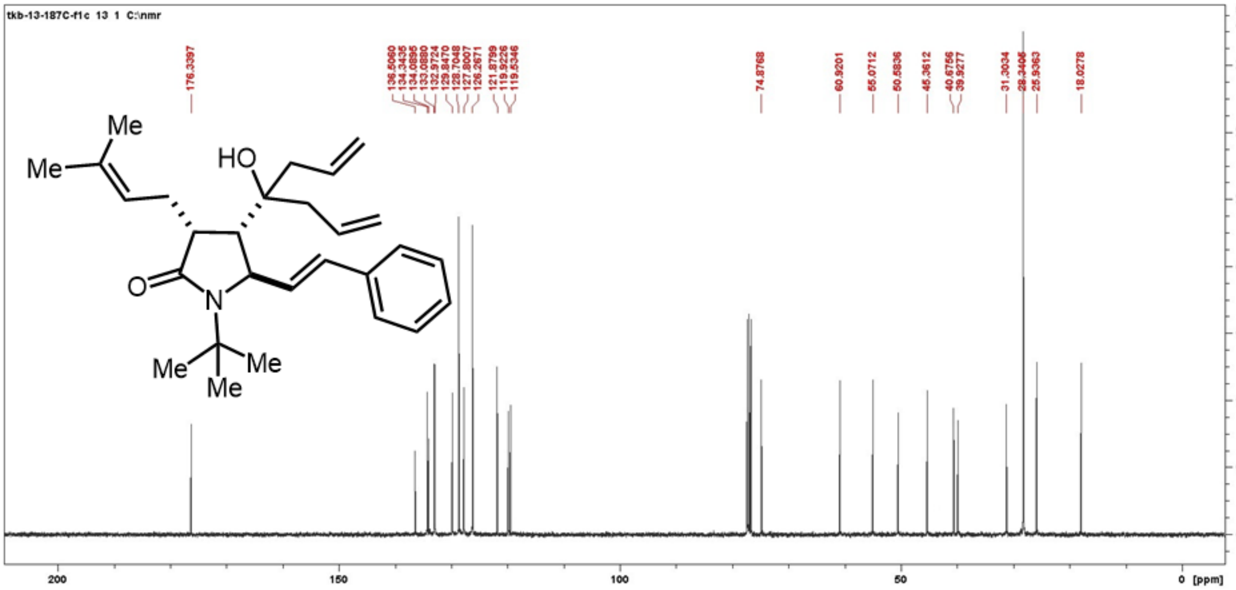
8a; 83%, >99:1 dr

E^+ = prenyl bromide

Compound 8a

Prepared in 0.50 mmol scale using **General Procedures C** and **D**. Grignard reagent = allylmagnesium bromide and electrophile = prenyl bromide. Purification: Flash chromatography on silica eluting with hexane/acetone (95:5 to 80:20). Yellowish oil. Yield = 175.0 mg, 83%, >99:1 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.30 (m, 4H), 7.33 – 7.23 (m, 1H), 6.52 (d, *J* = 16.0 Hz, 1H), 6.24 (dd, *J* = 16.0, 8.5 Hz, 1H), 5.95 – 5.77 (m, 2H), 5.24 – 5.09 (m, 5H), 4.57 (dd, *J* = 8.5, 1.6 Hz, 1H), 2.54 – 2.40 (m, 2H), 2.43 – 2.19 (m, 5H), 1.93 (dd, *J* = 5.1, 3.1 Hz, 2H), 1.74 (d, *J* = 1.4 Hz, 3H), 1.61 (d, *J* = 1.4 Hz, 3H), 1.48 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.34, 136.51, 134.35, 134.09, 133.09, 132.98, 129.85, 128.71, 127.80, 126.27, 121.88, 119.93, 119.54, 74.88, 60.92, 55.08, 50.59, 45.36, 40.68, 39.93, 31.31, 28.34, 25.94, 18.03. **HRMS-EI**$^+$ (*m/z*): calc for $C_{28}H_{29}NO_2$ $[M]^+$ 421.2981, found 421.2988.





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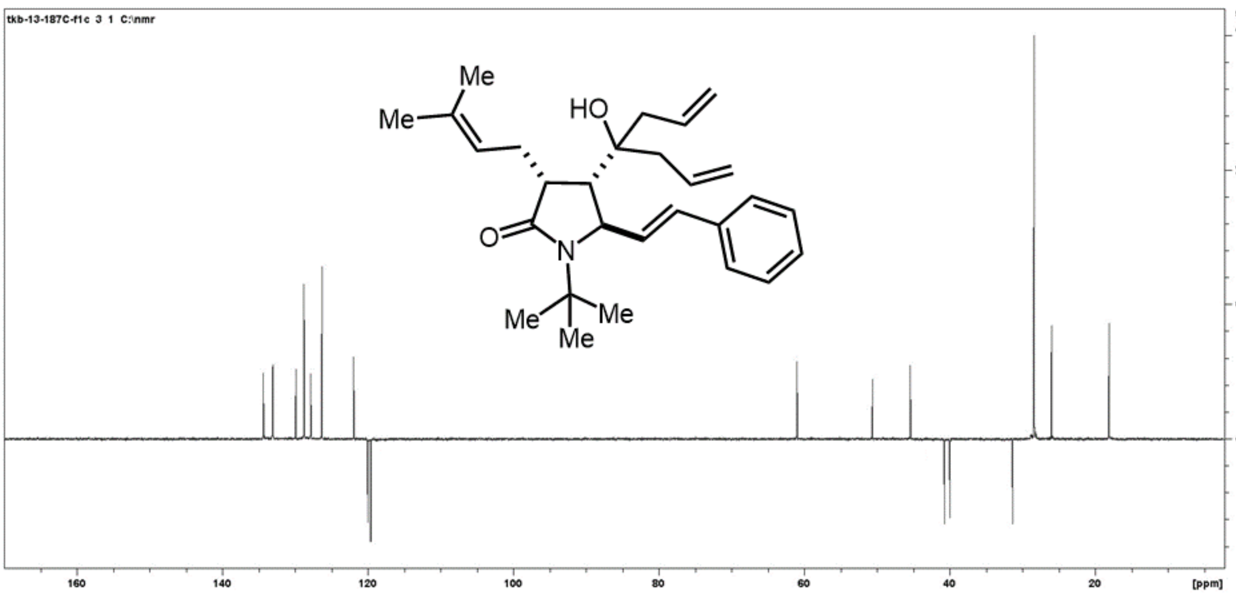

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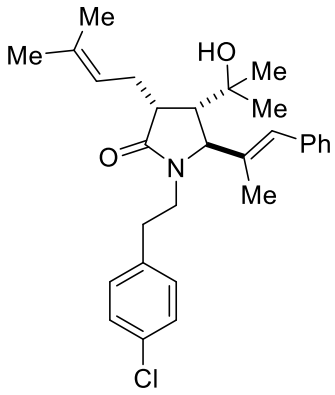
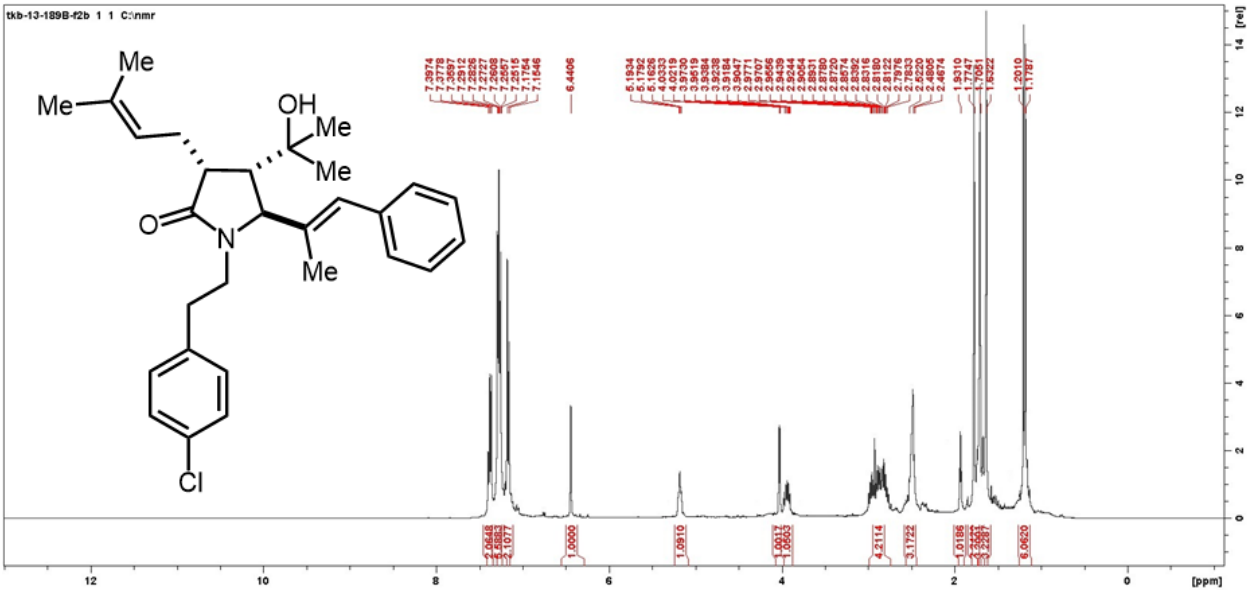


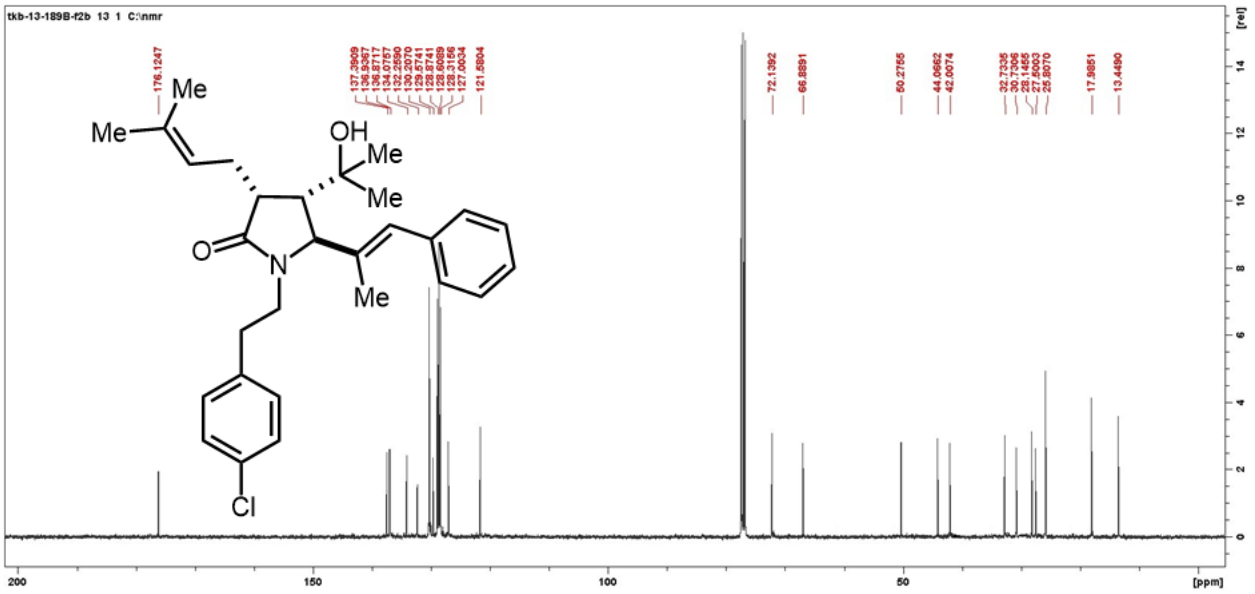
8b; 80%, >99:1 dr

E^+ = prenyl bromide

Compound 8b

Prepared in 0.50 mmol scale using **General Procedures C** and **D**. Grignard reagent = methylmagnesium bromide and electrophile = prenyl bromide. Purification: Flash chromatography on silica eluting with hexane/acetone (95:5 to 80:20). Yellowish oil. Yield = 186.4 mg, 80%, >99:1 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.16 (m, 9H), 6.44 (s, 1H), 5.19 – 5.16 (m, 1H), 4.03 (d, J = 4.6 Hz, 1H), 3.94 (ddd, J = 12.4, 8.2, 6.1 Hz, 1H), 3.04 – 2.72 (m, 4H), 2.60 – 2.42 (m, 3H), 1.93 (t, J = 4.6 Hz, 1H), 1.80 – 1.48 (m, 9H), 1.20 (s, 3H), 1.18 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.13, 137.39, 136.94, 136.88, 134.08, 132.26, 130.21, 129.58, 128.88, 128.61, 128.59, 128.32, 127.01, 121.58, 72.14, 66.89, 50.28, 44.07, 42.01, 32.74, 30.73, 28.15, 27.50, 25.81, 17.99, 13.45. **HRMS-EI**$^+$ (*m/z*): calc for $C_{29}H_{36}ClNO_2$ $[M]^+$ 465.2435, found 465.2439.

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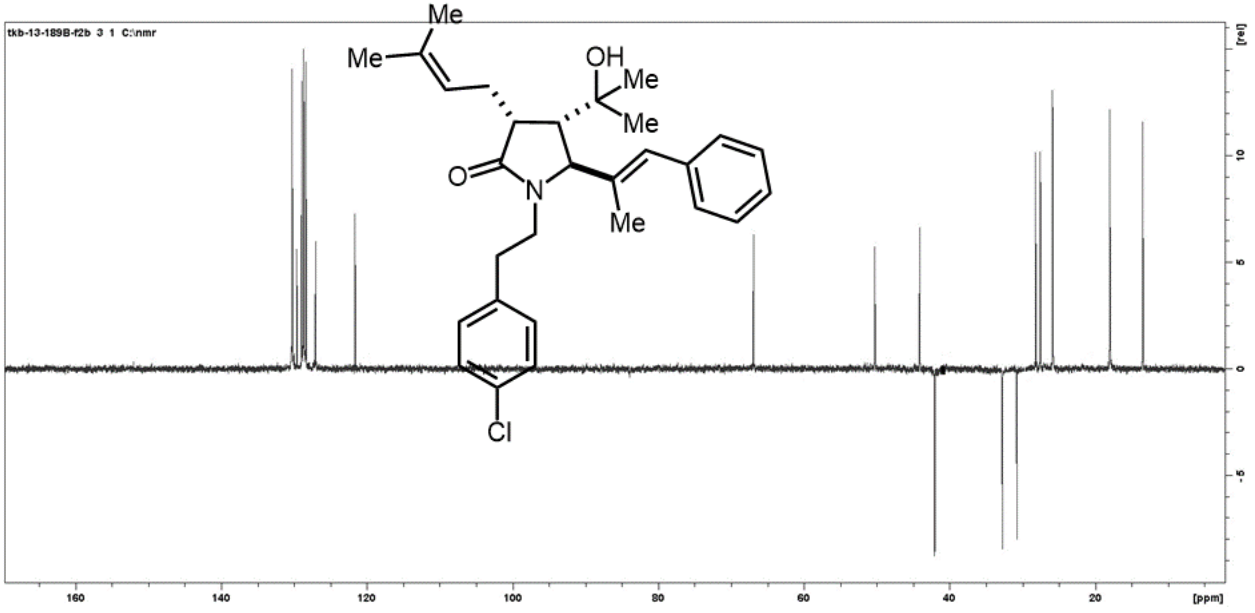
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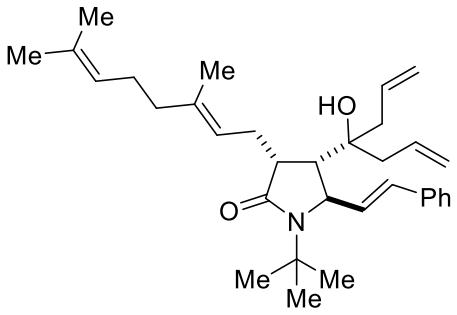
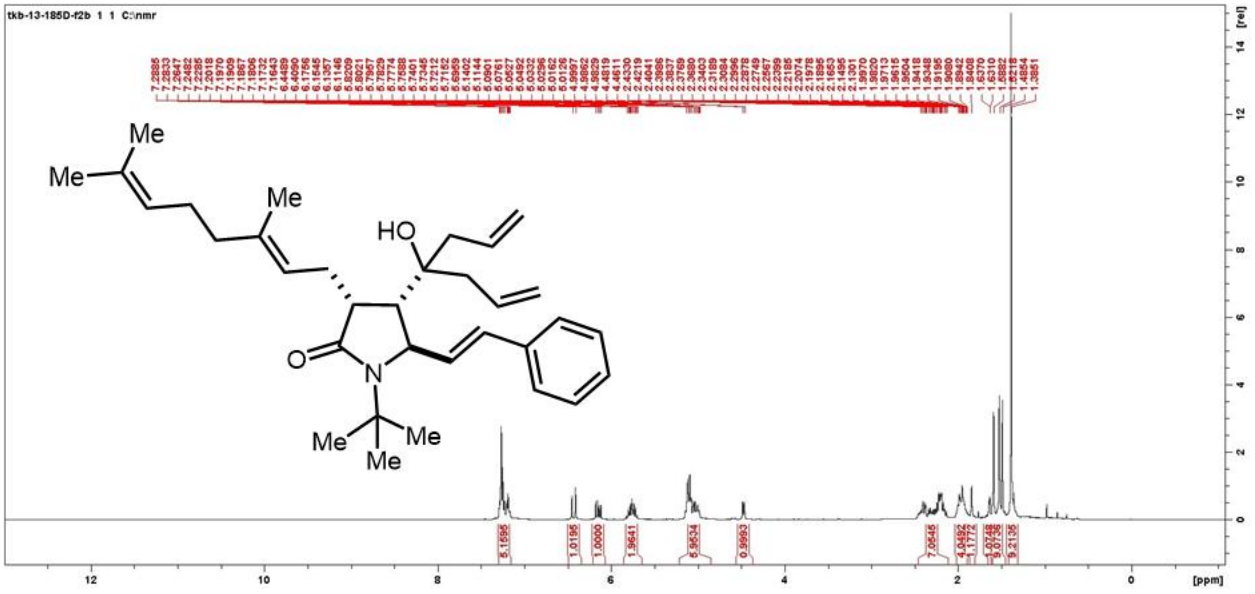
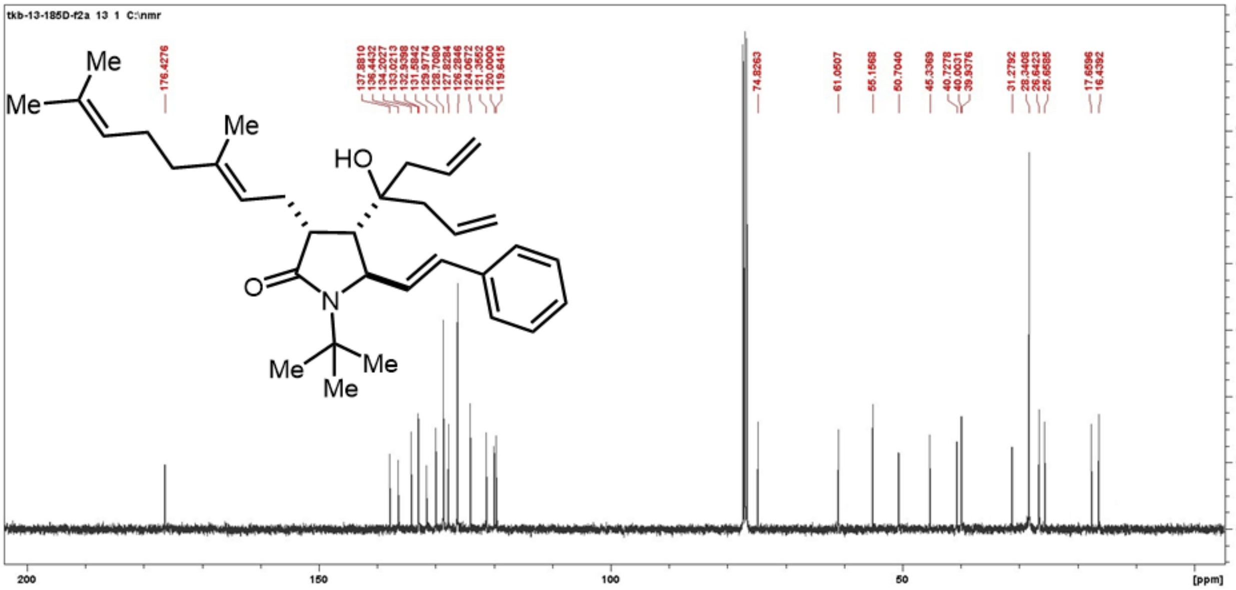


8c; 79%, 95:5 dr
E^+ = geranyl bromide

Compound 8c

Prepared in 0.50 mmol scale using **General Procedures C** and **D**. Grignard reagent = allylmagnesium bromide and electrophile = geranyl bromide. Purification: Flash chromatography on silica eluting with hexane/acetone (95:5 to 80:20). Yellowish oil. Yield = 193.4 mg, 79%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.14 (m, 5H), 6.43 (d, *J* = 15.9 Hz, 1H), 6.15 (dd, *J* = 16.0, 8.4 Hz, 1H), 5.76 (ddq, *J* = 17.8, 10.3, 7.6 Hz, 2H), 5.18 – 5.07 (m, 6H), 4.47 (dd, *J* = 8.4, 1.7 Hz, 1H), 2.49 – 2.09 (m, 7H), 1.96 (ttd, *J* = 16.3, 10.0, 6.5 Hz, 4H), 1.84 (d, *J* = 2.1 Hz, 1H), 1.61 (d, *J* = 2.0 Hz, 3H), 1.50 (d,d, *J* = 1.4 Hz, 5H), 1.39 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.39, 137.85, 136.47, 134.27, 133.06, 132.97, 131.57, 129.94, 128.71, 127.82, 126.29, 124.08, 121.38, 119.97, 119.61, 74.84, 61.00, 55.10, 50.70, 45.35, 40.74, 40.02, 39.94, 31.28, 28.35, 26.65, 25.66, 17.66, 16.44. **HRMS-EI$^+$** (*m/z*): calc for $C_{33}H_{47}NO_2$ $[M]^+$ 489.3607, found 489.3612.

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Me
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O
N
Me
Me
Me
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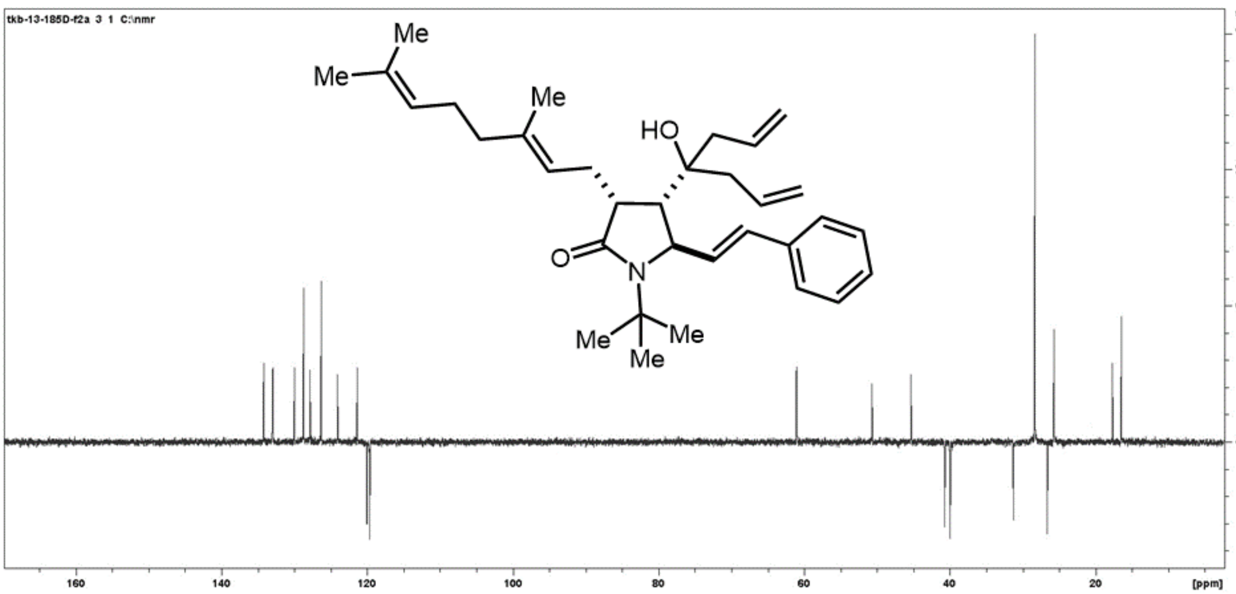
[ppm]


tkb-13-185D-f2a 3 1 C:\nmr
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Me
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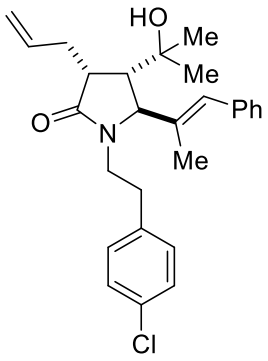
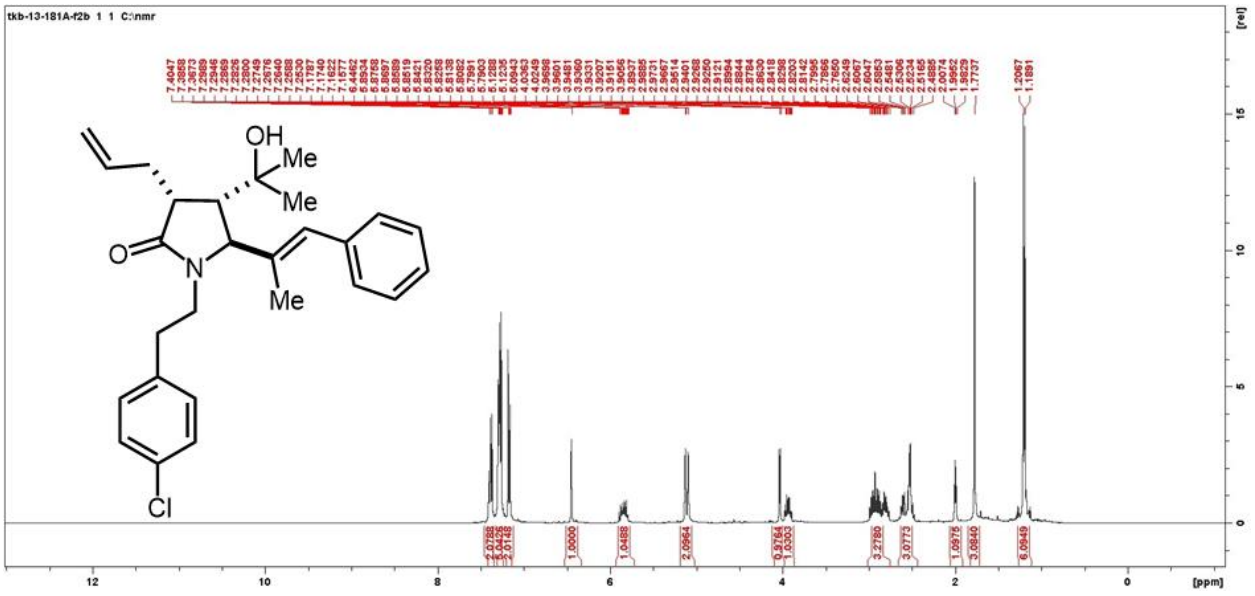
[rel]
[ppm]

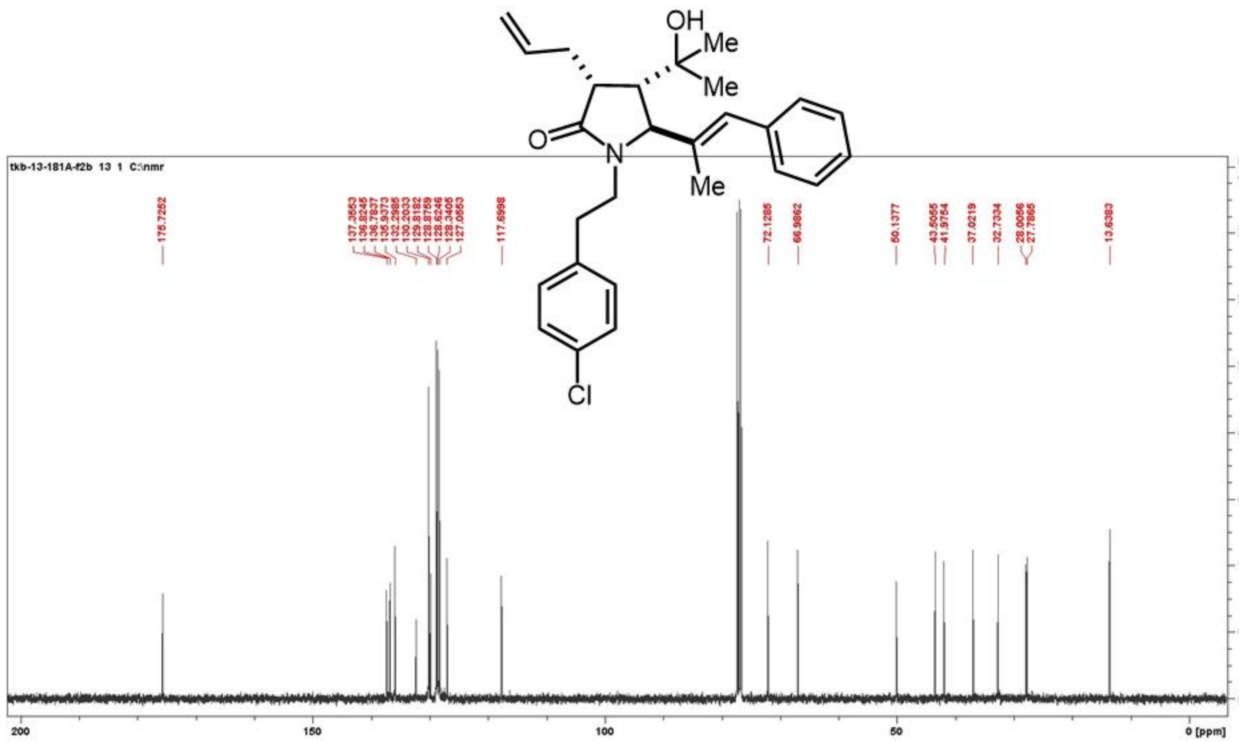


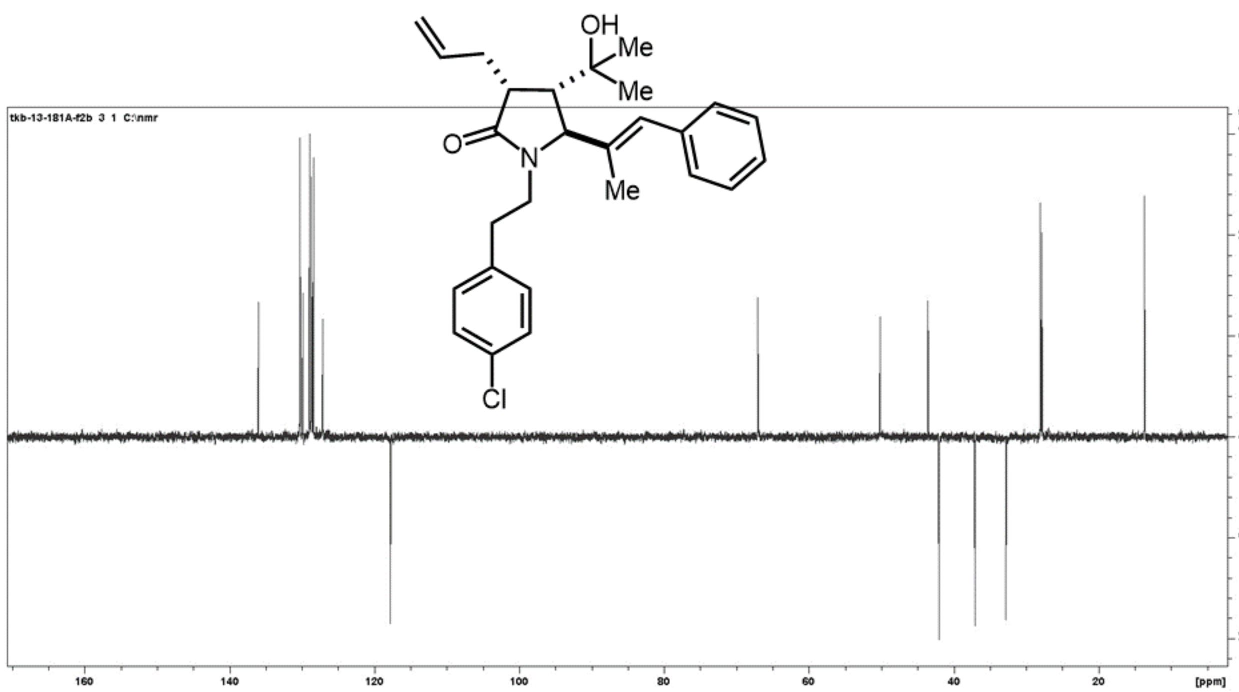
8d; 89%, 95:5 dr
E^+ = allyl bromide

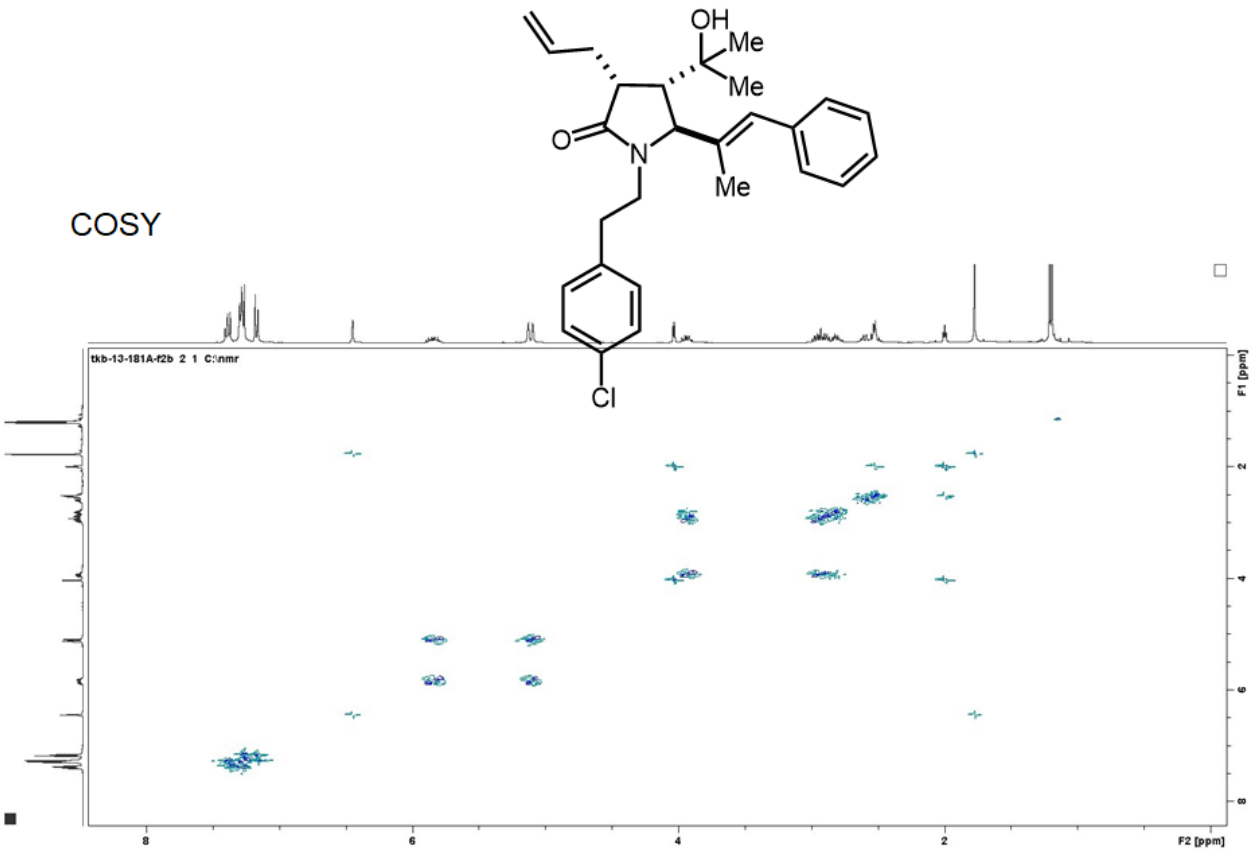
Compound 8d

Prepared in 0.50 mmol scale using **General Procedures C** and **D**. Grignard reagent = methylmagnesium bromide and electrophile = allyl bromide. Purification: Flash chromatography on silica eluting with hexane/acetone (95:5 to 80:20). Yellowish oil. Yield = 194.9 mg, 89%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 – 7.33 (m, 2H), 7.28 (ddt, *J* = 8.9, 7.6, 2.3 Hz, 5H), 7.20 – 7.13 (m, 2H), 6.45 (d, *J* = 1.7 Hz, 1H), 5.92 – 5.77 (m, 1H), 5.16 – 5.06 (m, 2H), 4.03 (d, *J* = 4.6 Hz, 1H), 3.99 – 3.87 (m, 1H), 3.01 – 2.84 (m, 2H), 2.86 – 2.74 (m, 1H), 2.68 – 2.54 (m, 1H), 2.57 – 2.45 (m, 2H), 2.00 (t, *J* = 4.9 Hz, 1H), 1.77 (d, *J* = 1.3 Hz, 3H), 1.20 (s,s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.73, 137.36, 136.83, 136.79, 135.94, 132.30, 130.21, 129.82, 128.88, 128.63, 128.34, 127.06, 117.70, 72.13, 66.99, 50.14, 43.51, 41.98, 37.03, 32.74, 28.01, 27.79, 13.64. **HRMS-EI**$^+$ (*m/z*): calc for $C_{27}H_{32}ClNO_2$ $[M]^+$ 437.2122, found 437.2126.





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OH
Me
Me
O
N
Me
Cl
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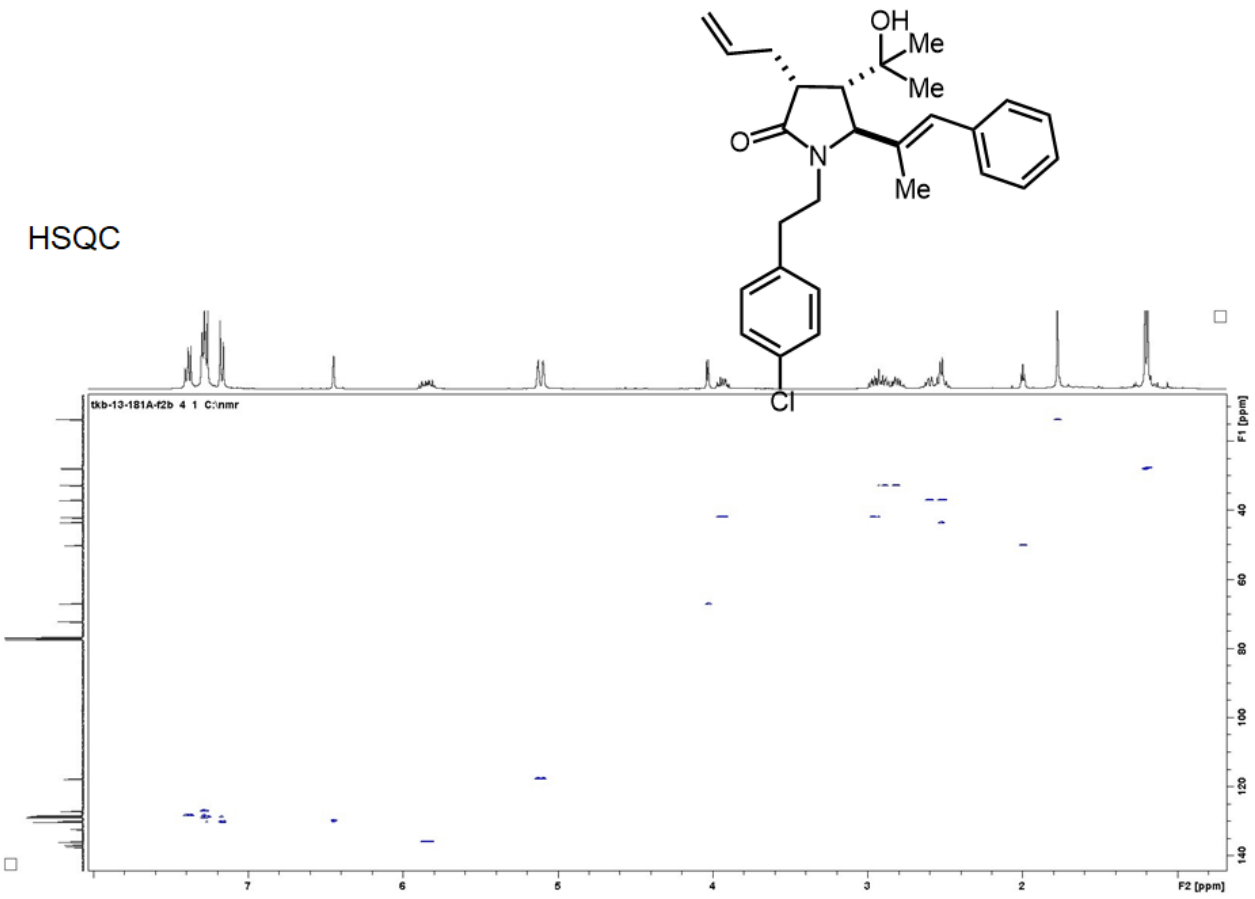
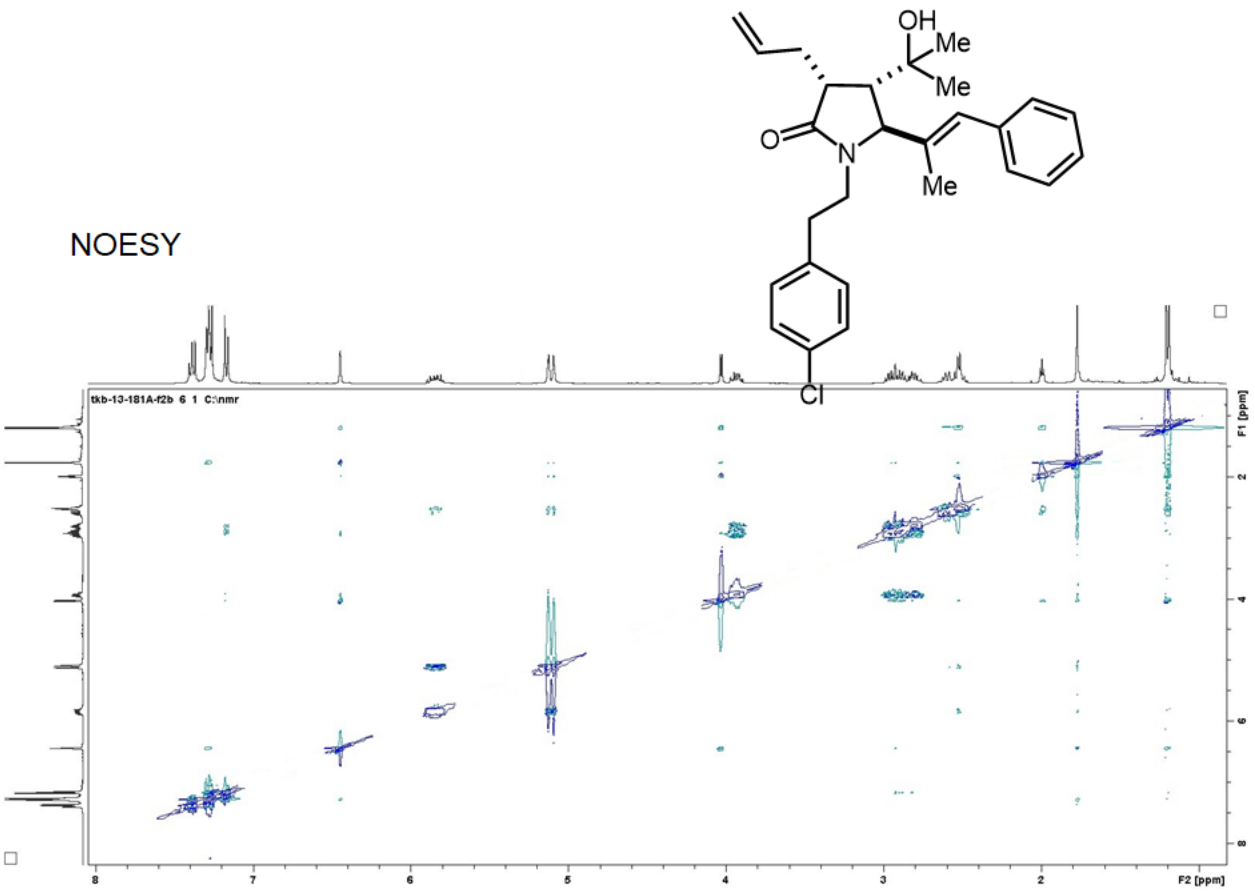
F1 [ppm]
F2 [ppm]
8
6
4
2

HSQC



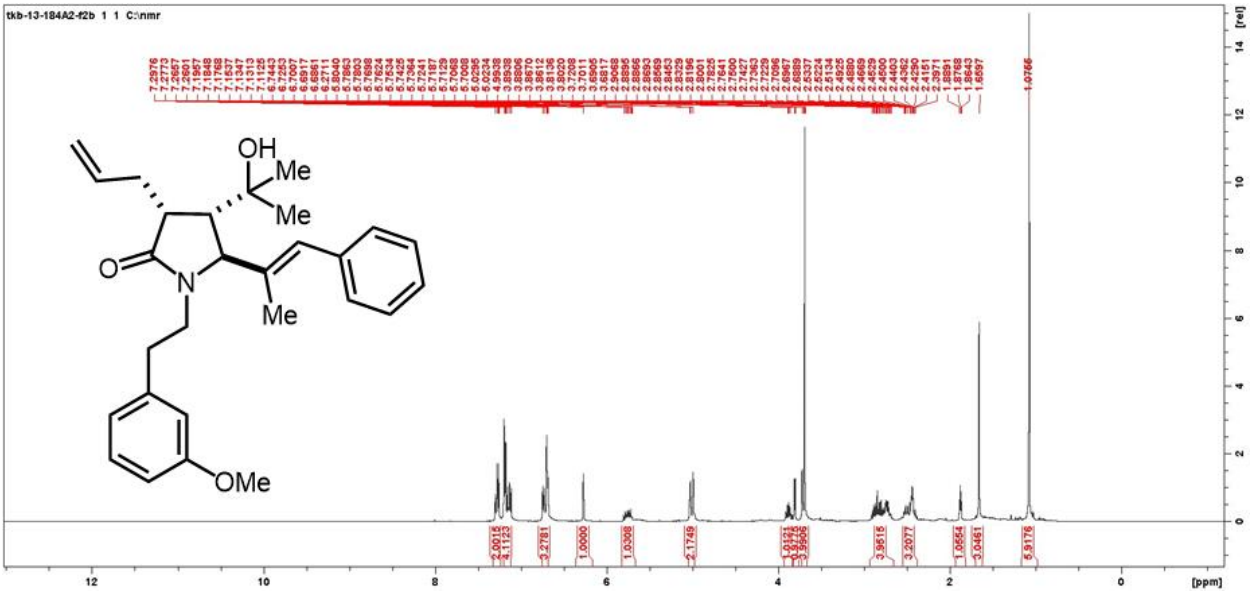


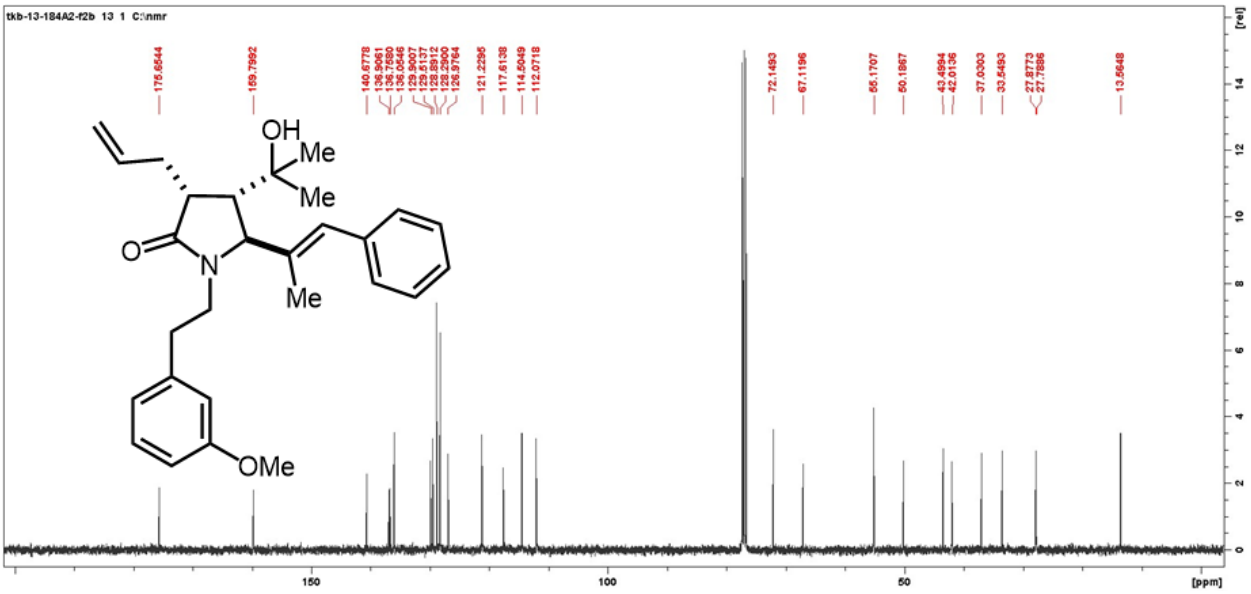
8e; 91%, 95:5 dr
E^+ = allyl bromide

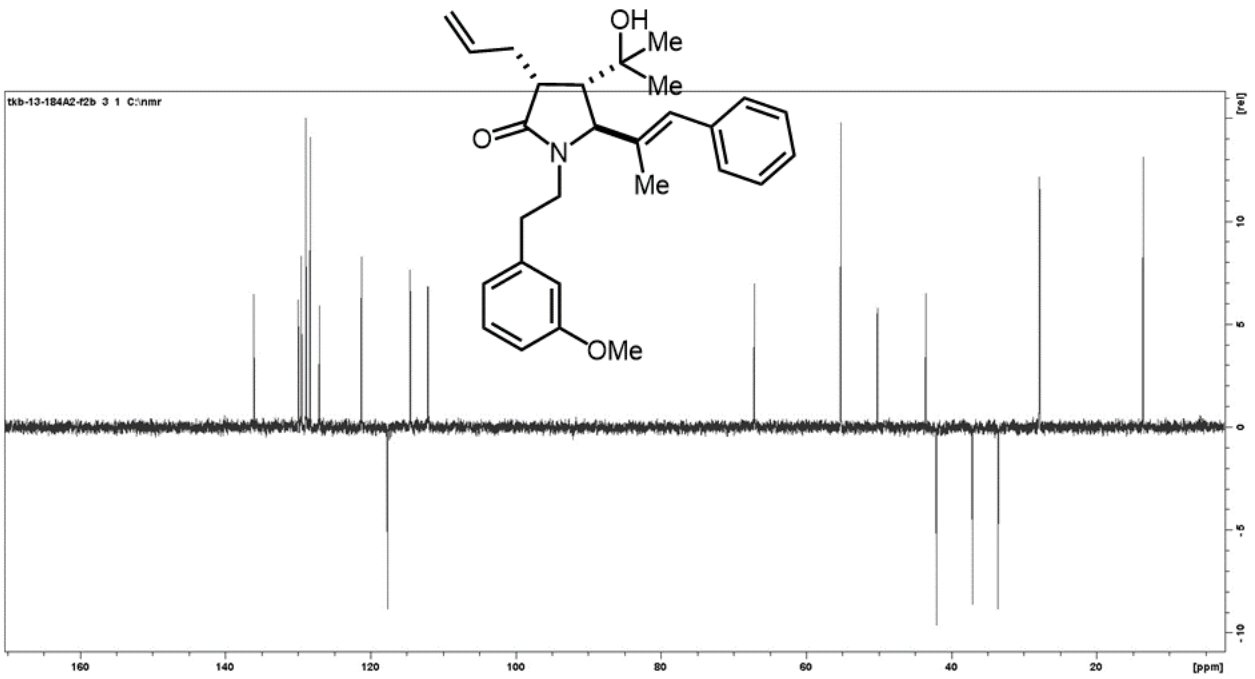
Compound 8e

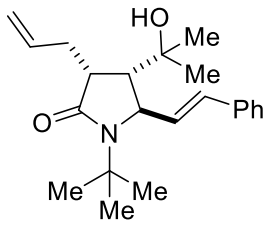
Prepared in 0.50 mmol scale using **General Procedures C** and **D**. Grignard reagent = methylmagnesium bromide and electrophile = allyl bromide. Purification: Flash chromatography on silica eluting with hexane/acetone (95:5 to 70:30). Yellowish oil. Yield = 197.3 mg, 91%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.22 (m, 2H), 7.22 – 7.03 (m, 4H), 6.77 – 6.66 (m, 3H), 6.27 (s, 1H), 5.83 – 5.68 (m, 1H), 5.01 (dq, *J* = 13.3, 1.7 Hz, 3H), 3.94 – 3.83 (m, 1H), 3.81 (d, *J* = 4.6 Hz, 1H), 3.69 (s, 3H), 2.93 – 2.65 (m, 4H), 2.58 – 2.42 (m, 3H), 1.88 (t, *J* = 5.0 Hz, 1H),

1.66 (s, 3H), 1.08 (s,s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.66, 159.80, 140.68, 136.91, 136.76, 136.06, 129.90, 129.52, 128.89, 128.29, 126.98, 121.23, 117.62, 114.51, 112.08, 72.15, 67.12, 55.17, 50.19, 43.50, 42.02, 37.03, 33.55, 27.88, 27.79, 13.57. **HRMS-EI$^+$** (*m/z*): calc for $C_{28}H_{35}NO_3$ $[M]^+$ 433.2617, found 433.2611.





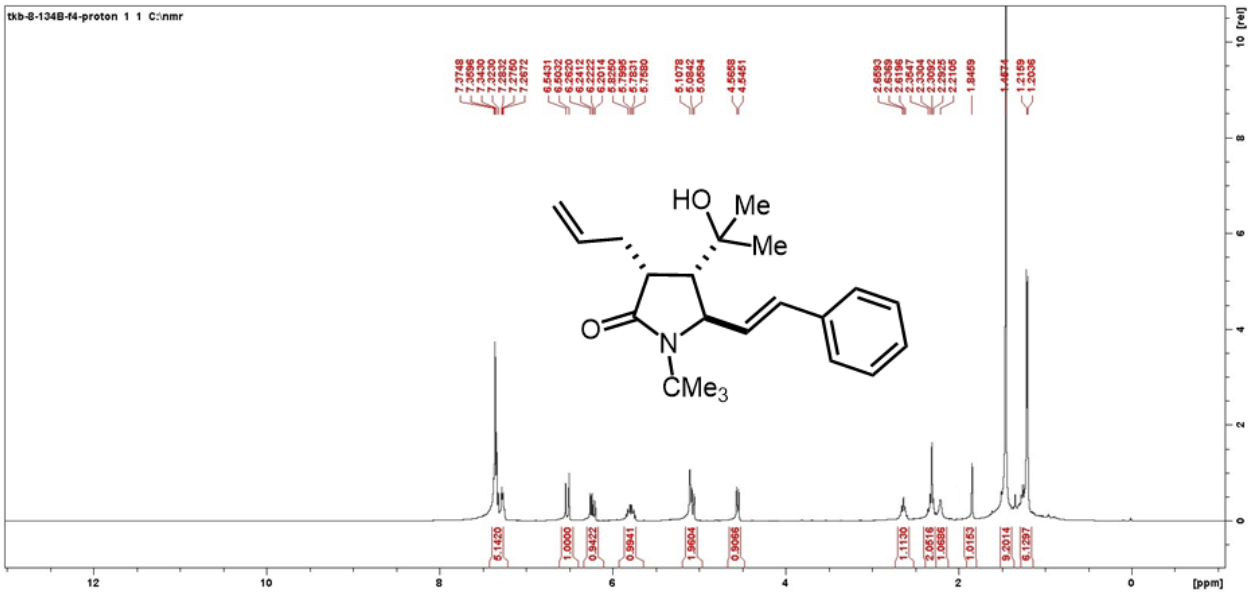




8f; 83%, 95:5 dr

Compound 8f

Prepared in 0.50 mmol scale using **General Procedures C** and **D**. Grignard reagent = methylmagnesium bromide and electrophile = allyl bromide. Purification: Flash chromatography on silica eluting with hexane/acetone (95:5 to 80:20). Yellowish oil. Yield = 141.7 mg, 83%, 95:5 dr. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.38 – 7.21 (m, 5H), 6.50 (d, *J* = 16.0 Hz, 1H), 6.21 (dd, *J* = 16.0, 8.3 Hz, 1H), 5.77 (ddd, *J* = 17.0, 10.5, 6.3 Hz, 1H), 5.11 – 5.02 (m, 2H), 4.53 (d, *J* = 8.3 Hz, 1H), 2.62 (t, *J* = 8.3 Hz, 1H), 2.28 (d, *J* = 6.8 Hz, 2H), 2.02 (d, *J* = 4.0 Hz, 1H), 1.82 (s, 1H), 1.44 (s, 9H), 1.19 (s,s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.12, 136.58, 136.13, 134.63, 129.77, 128.78, 127.87, 126.37, 117.73, 72.56, 61.43, 55.14, 53.77, 45.81, 37.76, 28.36, 27.84, 25.19. **HRMS-EI^{+}** (*m/z*): calc for $C_{22}H_{31}NO_2$ $[M]^{+}$ 341.2355, found 341.2358.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N
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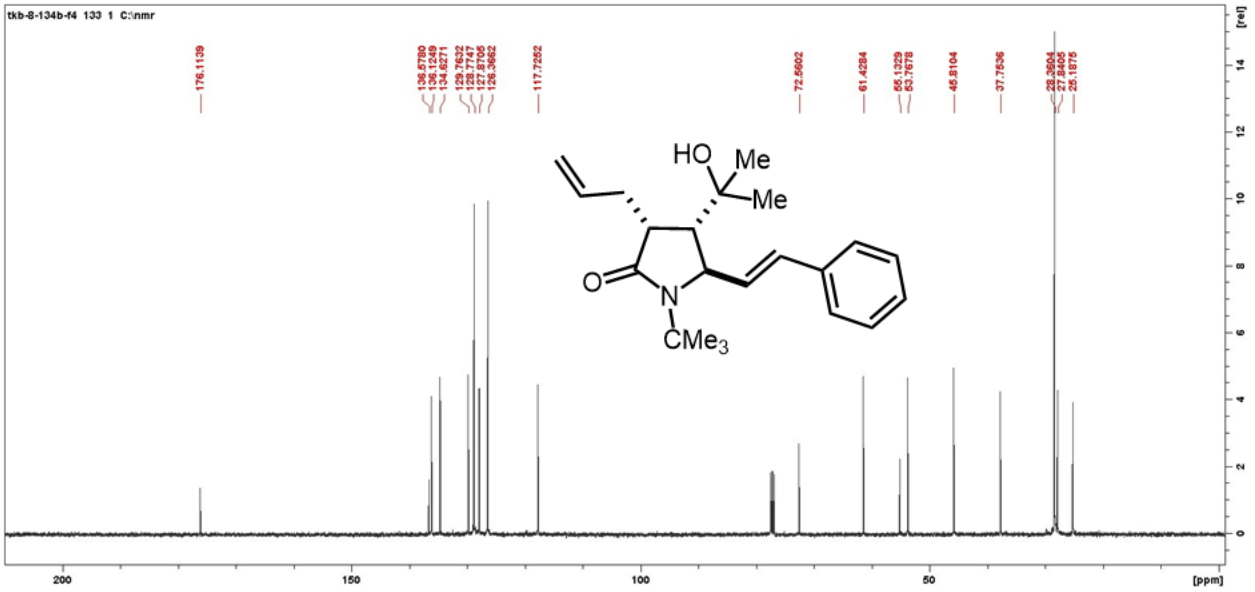
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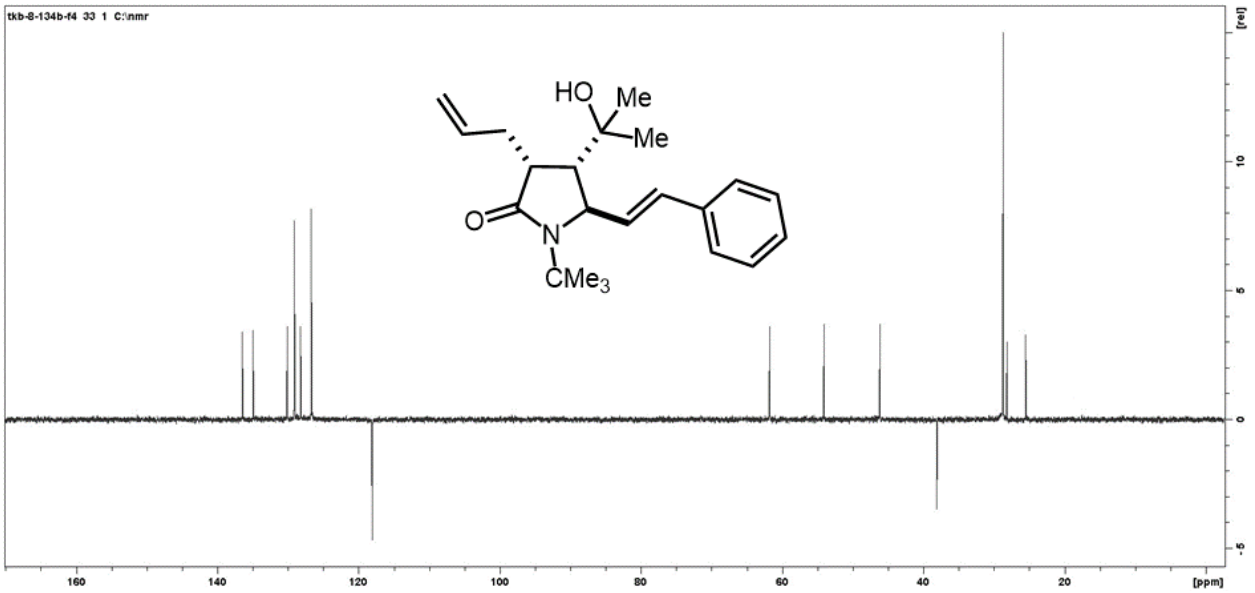
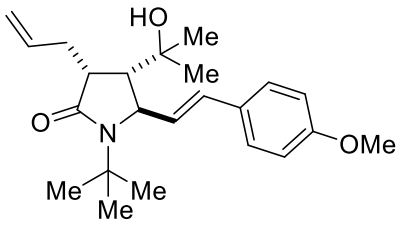
Me
O
N
CMe3
[ppm]

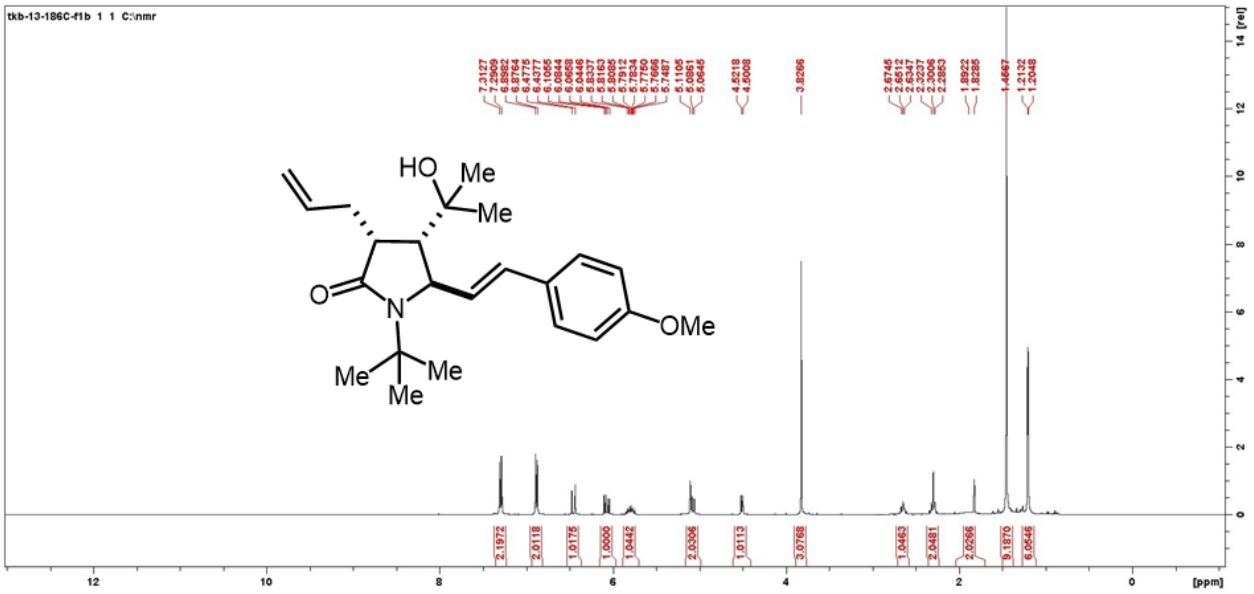




8g; 88%, 95:5 dr

Compound 8g

Prepared in 0.50 mmol scale using **General Procedures C** and **D**. Grignard reagent = methylmagnesium bromide and electrophile = allyl bromide. Purification: Flash chromatography on silica eluting with hexane/acetone (95:5 to 70:30). Yellowish oil. Yield = 163.5 mg, 88%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.2 Hz, 2H), 6.88 (d, *J* = 8.2 Hz, 2H), 6.46 (d, *J* = 15.9 Hz, 1H), 6.08 (dd, *J* = 15.9, 8.4 Hz, 1H), 5.87 – 5.73 (m, 1H), 5.13 – 5.04 (m, 2H), 4.55 – 4.48 (m, 1H), 3.83 (s, 3H), 2.72 – 2.59 (m, 1H), 2.37 – 2.22 (m, 2H), 1.83 (t, *J* = 1.8 Hz, 1H), 1.46 (s, 9H), 1.21 (s,s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.96, 159.43, 136.15, 132.31, 129.25, 129.21, 127.48, 117.59, 114.16, 72.60, 61.53, 55.35, 55.07, 53.90, 45.74, 37.72, 28.29, 27.76, 25.19. **HRMS-EI^{+}** (*m/z*): calc for $C_{23}H_{33}NO_3$ $[M]^{+}$ 371.2460, found 371.2468.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O
N
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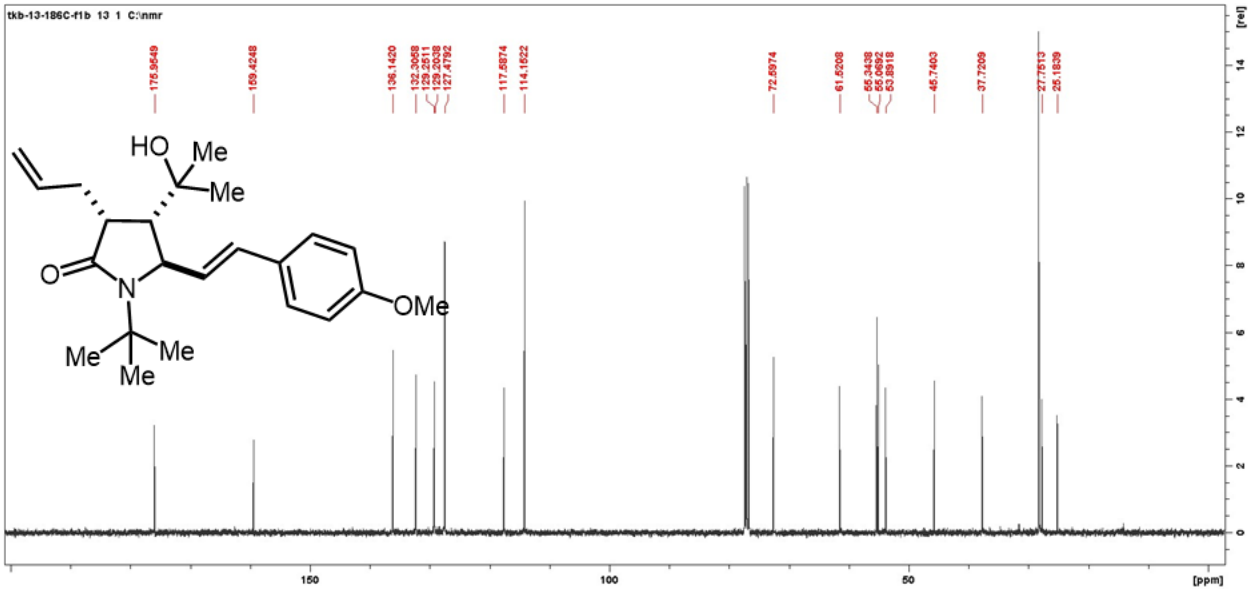
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55.0692
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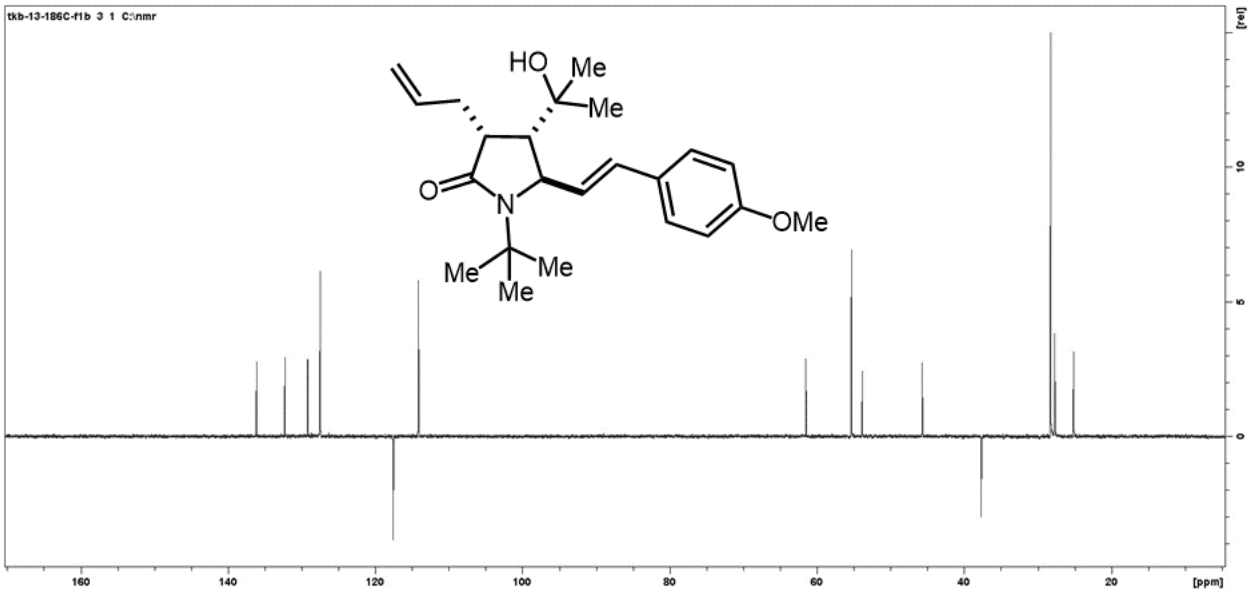
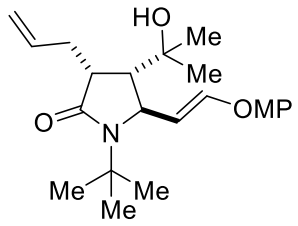
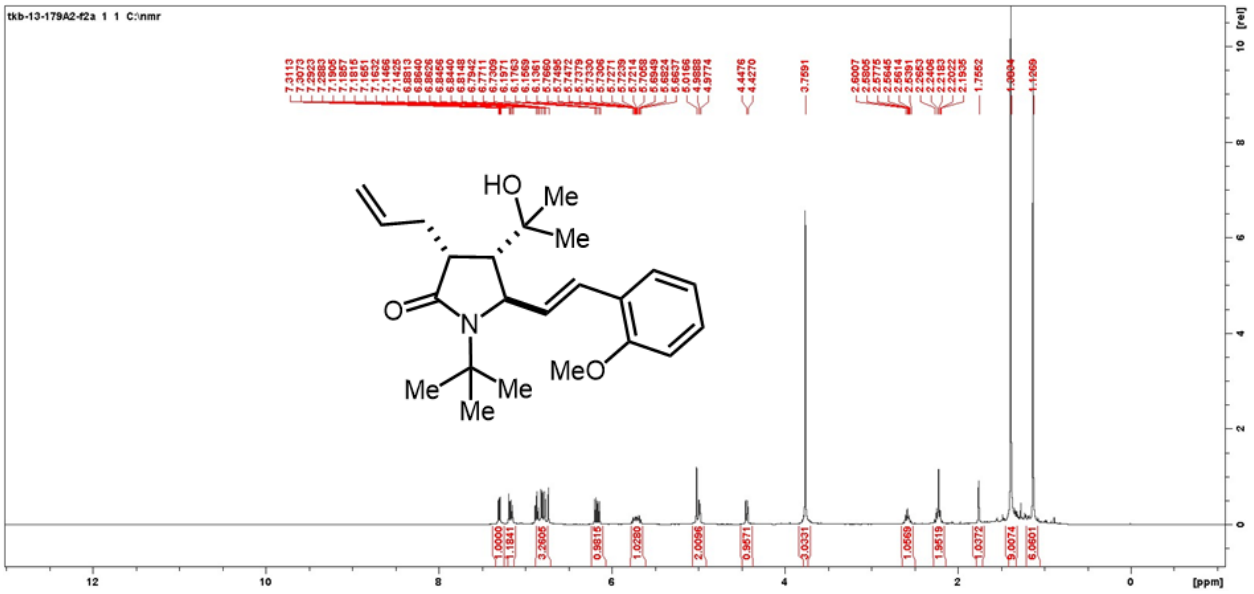




8h; 86%, 95:5 dr

Compound 8h

Prepared in 0.50 mmol scale using **General Procedures C** and **D**. Grignard reagent = methylmagnesium bromide and electrophile = allyl bromide. Purification: Flash chromatography on silica eluting with hexane/acetone (95:5 to 70:30). Yellowish oil. Yield = 159.7 mg, 86%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.16 (ddd, *J* = 8.1, 7.3, 1.7 Hz, 1H), 6.86 (td, *J* = 7.5, 1.1 Hz, 1H), 6.80 (dd, *J* = 8.2, 1.1 Hz, 1H), 6.75 (d, *J* = 16.1 Hz, 1H), 6.17 (dd, *J* = 16.1, 8.3 Hz, 1H), 5.79 – 5.64 (m, 1H), 5.04 – 4.95 (m, 2H), 4.44 (dd, *J* = 8.4, 1.2 Hz, 1H), 3.76 (s, 3H), 2.57 (tdd, *J* = 10.5, 5.2, 3.6 Hz, 1H), 2.29 – 2.16 (m, 2H), 1.76 (s, 1H), 1.30 (s, 9H), 1.13 (s,s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.99, 156.87, 136.26, 135.12, 128.77, 126.79, 125.59, 124.80, 120.68, 117.50, 110.97, 72.66, 61.81, 55.44, 55.06, 53.87, 45.82, 37.71, 28.28, 27.63, 25.29. **HRMS-EI^{+}** (*m/z*): calc for $C_{23}H_{33}NO_3$ $[M]^{+}$ 371.2460, found 371.2468.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Me
O
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MeO
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Me
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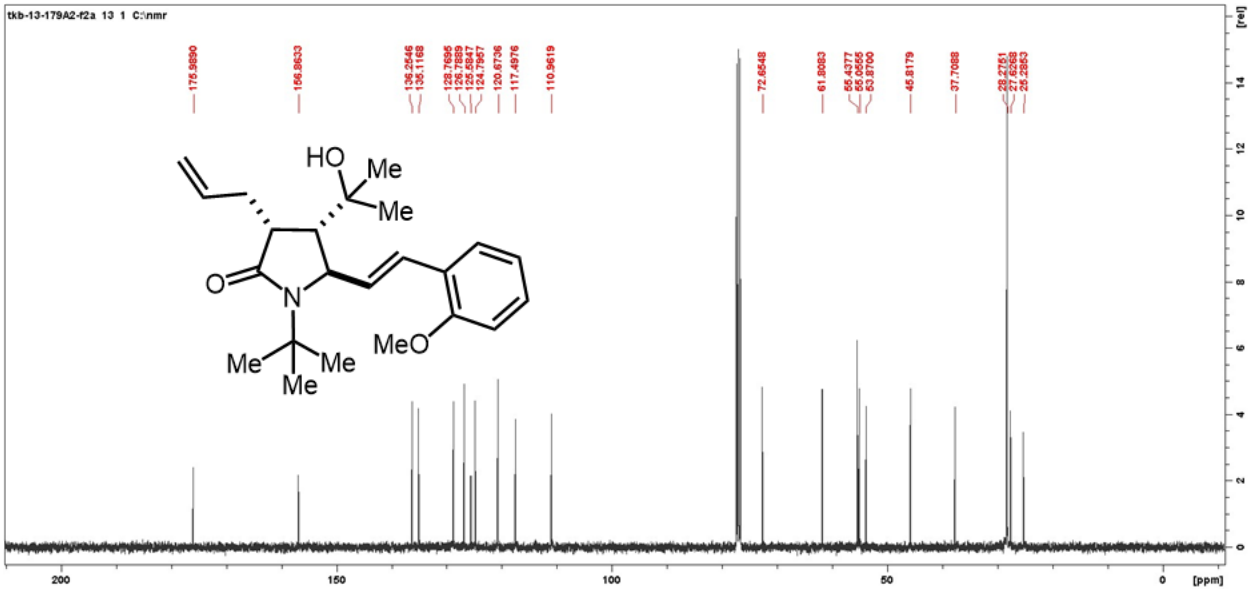
[rel]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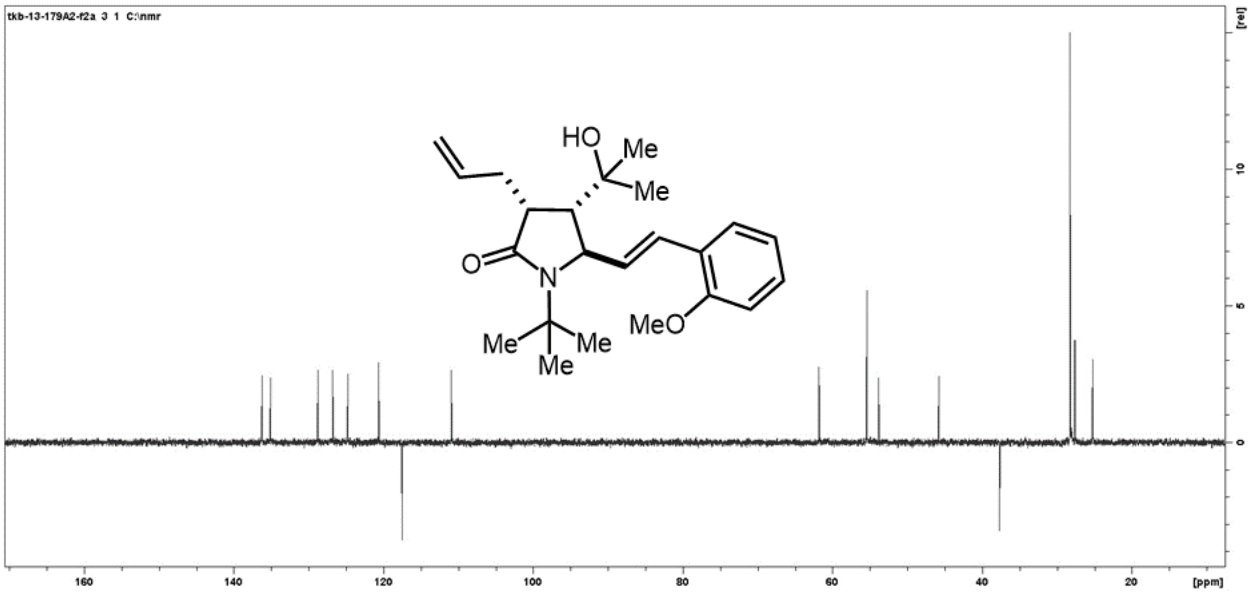
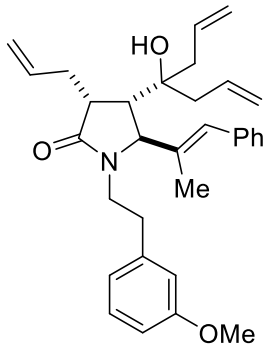
[rel]



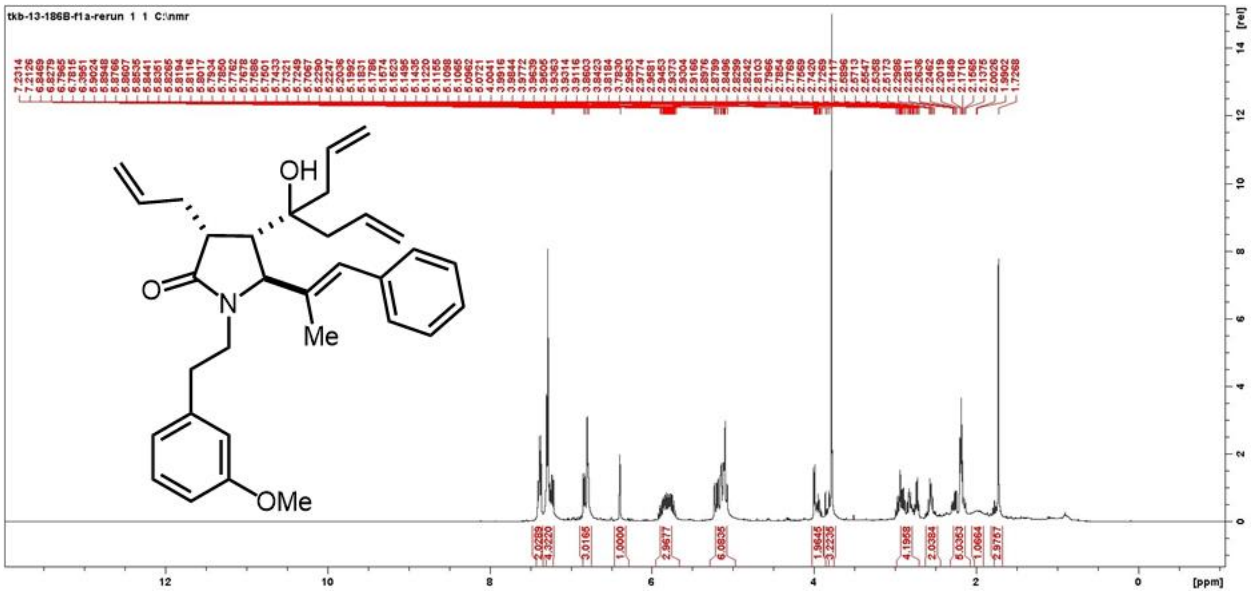


8i; 87%, 95:5 dr

E^+ = allyl bromide

Compound 8i

Prepared in 0.50 mmol scale using **General Procedures C** and **D**. Grignard reagent = allylmagnesium bromide and electrophile = allyl bromide. Purification: Flash chromatography on silica eluting with hexane/acetone (95:5 to 50:50). Yellowish oil. Yield = 211.3 mg, 87%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.19 (m, 6H), 6.87 – 6.76 (m, 3H), 6.34 (s, 1H), 5.94 – 5.68 (m, 3H), 5.23 – 5.07 (m, 6H), 4.03 – 3.89 (m, 2H), 3.78 (s, 3H), 3.02 – 2.68 (m, 4H), 2.56 (h, *J* = 7.3 Hz, 2H), 2.42 – 2.18 (m, 5H), 2.21 – 2.12 (m, 1H), 1.73 (d, *J* = 1.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.46, 159.78, 140.71, 136.80, 136.39, 136.00, 132.80, 132.78, 130.72, 129.50, 128.90, 128.33, 127.05, 121.25, 119.95, 119.62, 117.71, 114.56, 112.03, 74.67, 66.85, 55.15, 45.92, 42.48, 41.93, 41.45, 40.86, 36.88, 33.60, 13.33. **HRMS-EI$^+$** (*m/z*): calc for $C_{32}H_{39}NO_3$ $[M]^+$ 485.2930, found 485.2937.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O
N
Me
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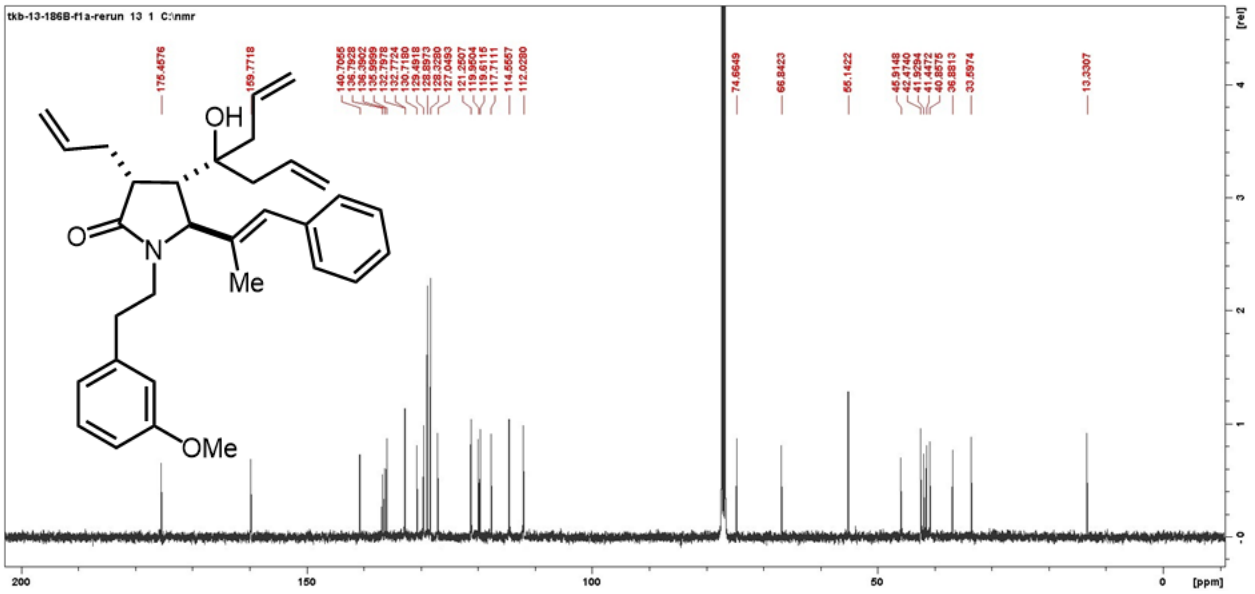
[ppm]
[rel]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OH
O
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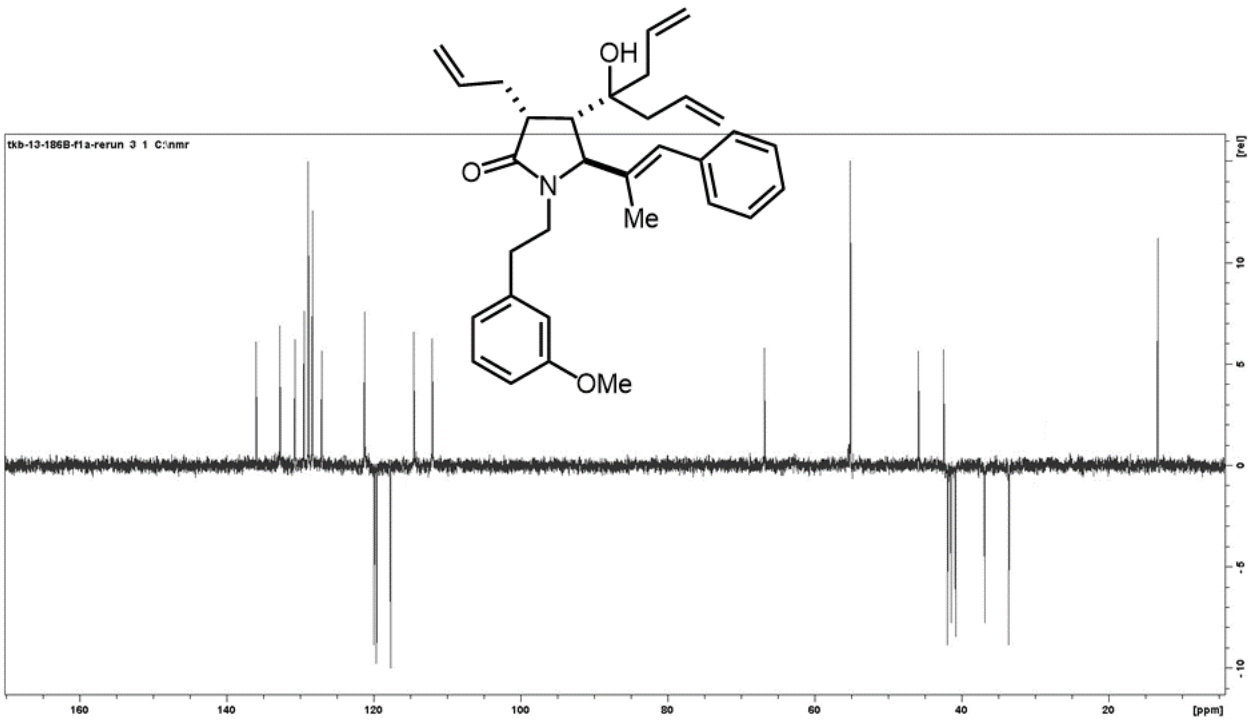
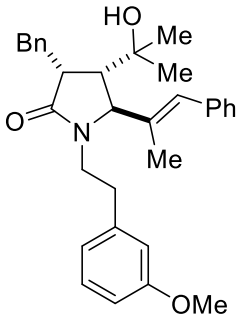


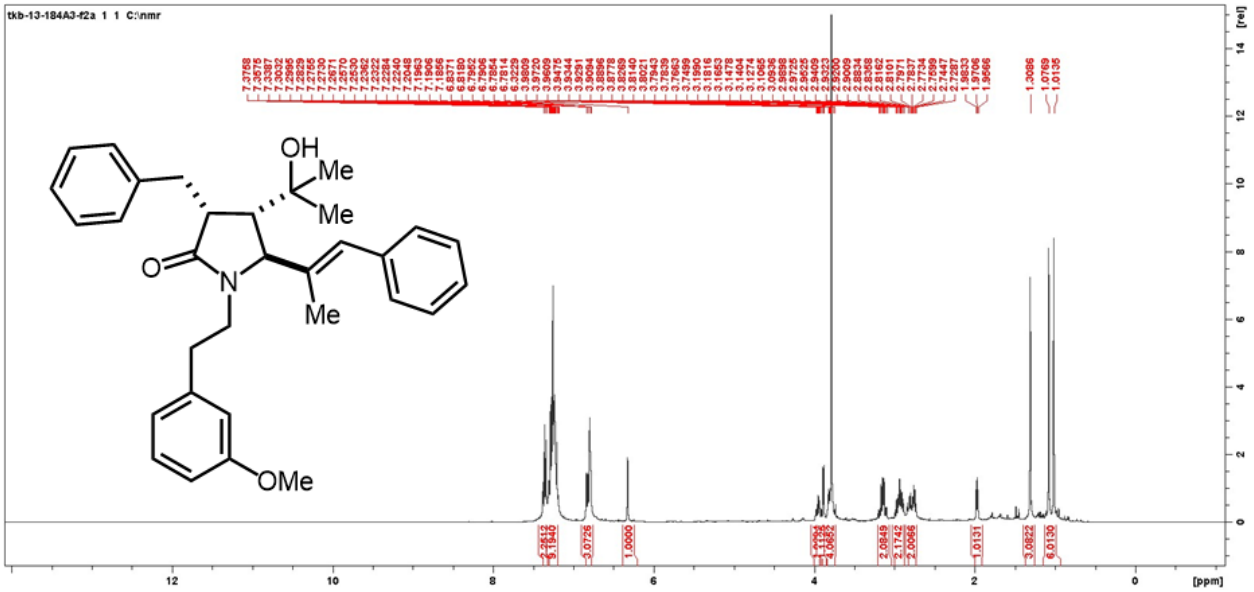


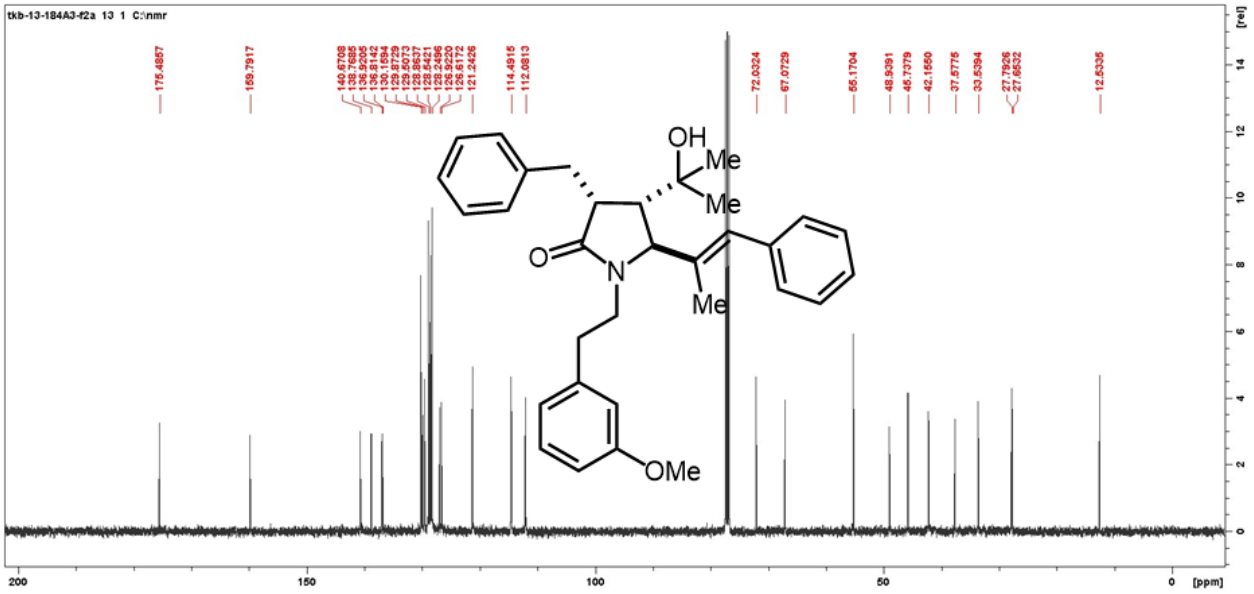
8j; 88%, 95:5 dr
E^+ = benyl bromide

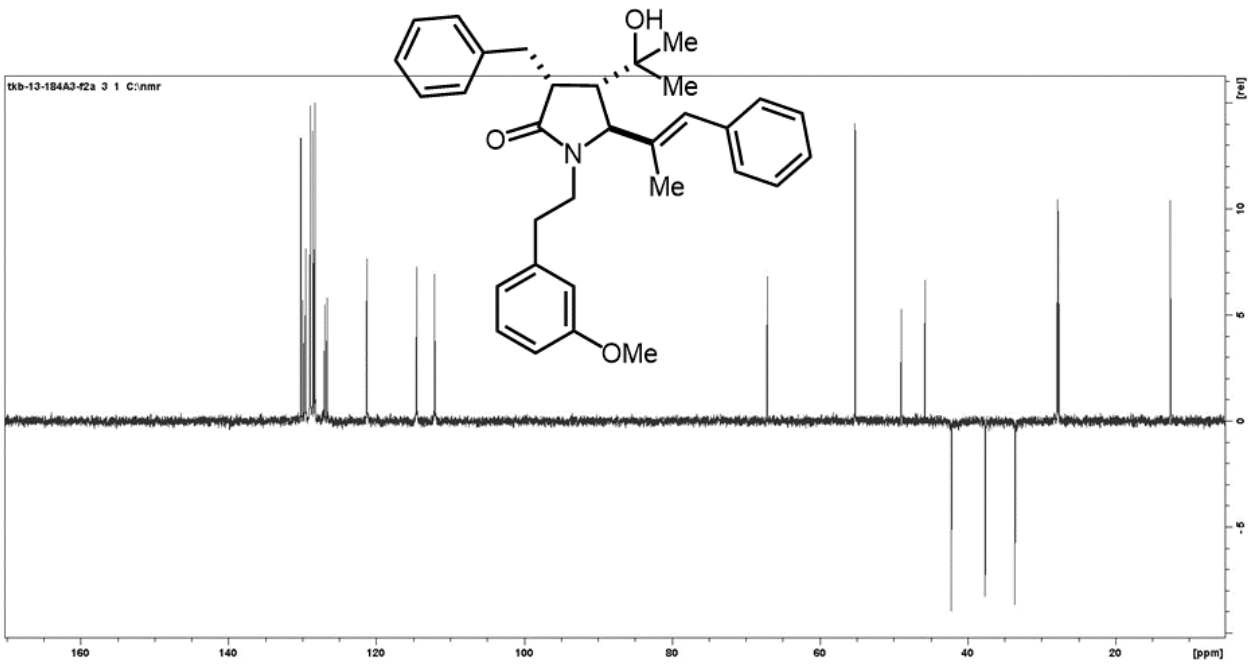
Compound 8j

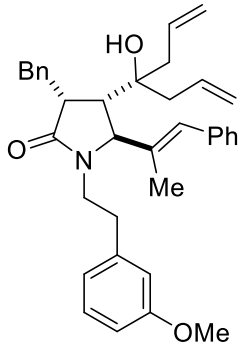
Prepared in 0.50 mmol scale using **General Procedures C** and **D**. Grignard reagent = methylmagnesium bromide and electrophile = benzyl bromide. Purification: Flash chromatography on silica eluting with hexane/acetone (95:5 to 50:50). Yellowish oil. Yield = 212.8 mg, 88%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.16 (m, 11H), 6.87 – 6.69 (m, 3H), 6.32 (s, 1H), 3.95 (ddd, *J* = 15.3, 9.0, 5.7 Hz, 1H), 3.88 (d, *J* = 4.8 Hz, 1H), 3.78 (s, 3H), 3.17 (dd, *J* = 13.5, 7.0 Hz, 1H), 3.12 (dd, *J* = 13.5, 5.2 Hz, 1H), 3.01 – 2.86 (m, 2H), 2.80 (td, *J* = 9.9, 5.9 Hz, 1H), 2.78 – 2.69 (m, 1H), 1.97 (dd, *J* = 5.9, 4.8 Hz, 1H), 1.31 (d, *J* = 1.3 Hz, 3H), 1.05 (s,s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.49, 159.80, 140.68, 138.77, 136.92, 136.82, 130.16, 129.88, 129.51, 128.87, 128.54, 128.25, 126.93, 126.62, 121.25, 114.50, 112.09, 72.03, 67.08,

55.17, 48.94, 45.74, 42.16, 37.58, 33.54, 27.80, 27.66, 12.54. **HRMS-EI$^+$** (*m/z*): calc for $C_{32}H_{37}NO_3$ $[M]^+$ 483.2773, found 483.2777.









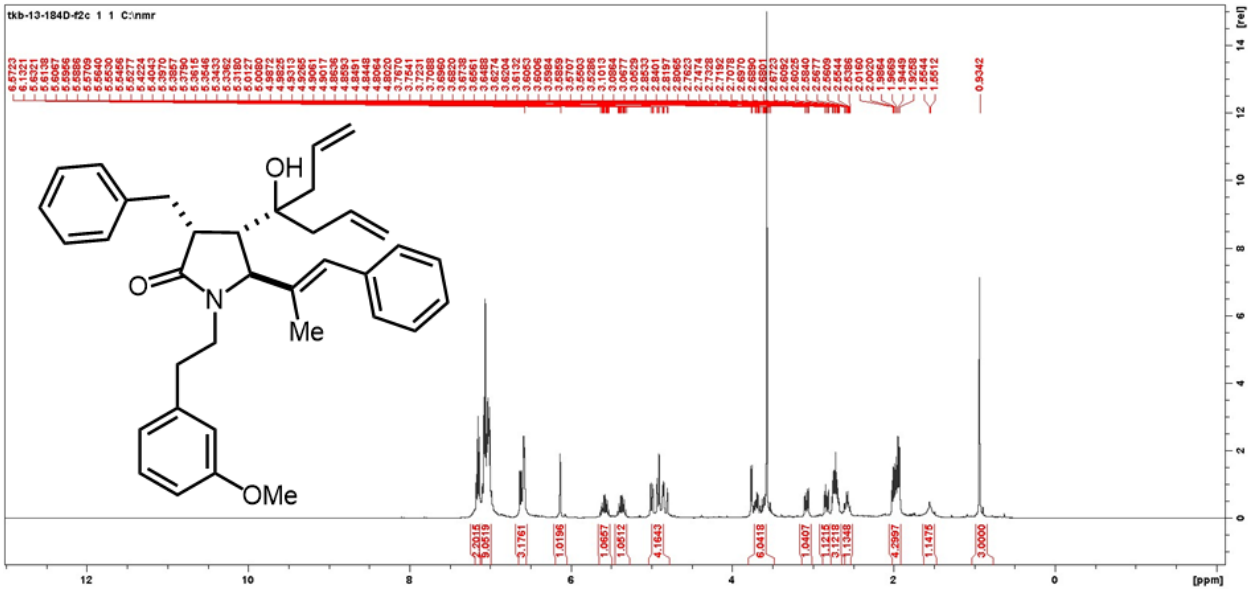
8k; 85%, 95:5 dr
E^+ = benzyl bromide

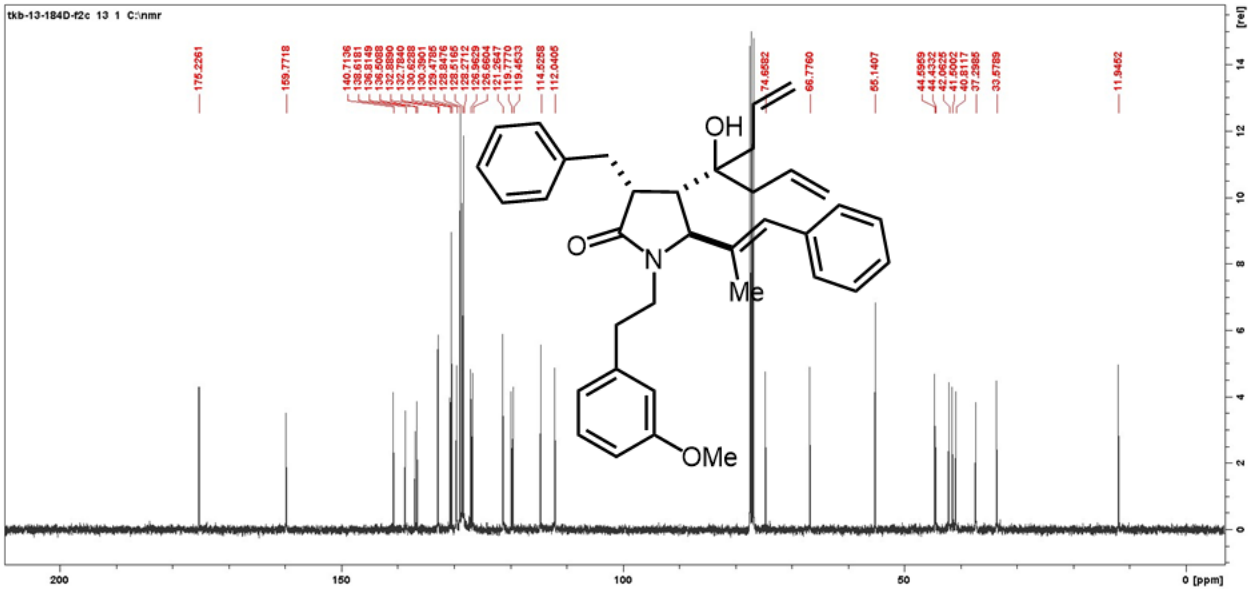
Compound 8k

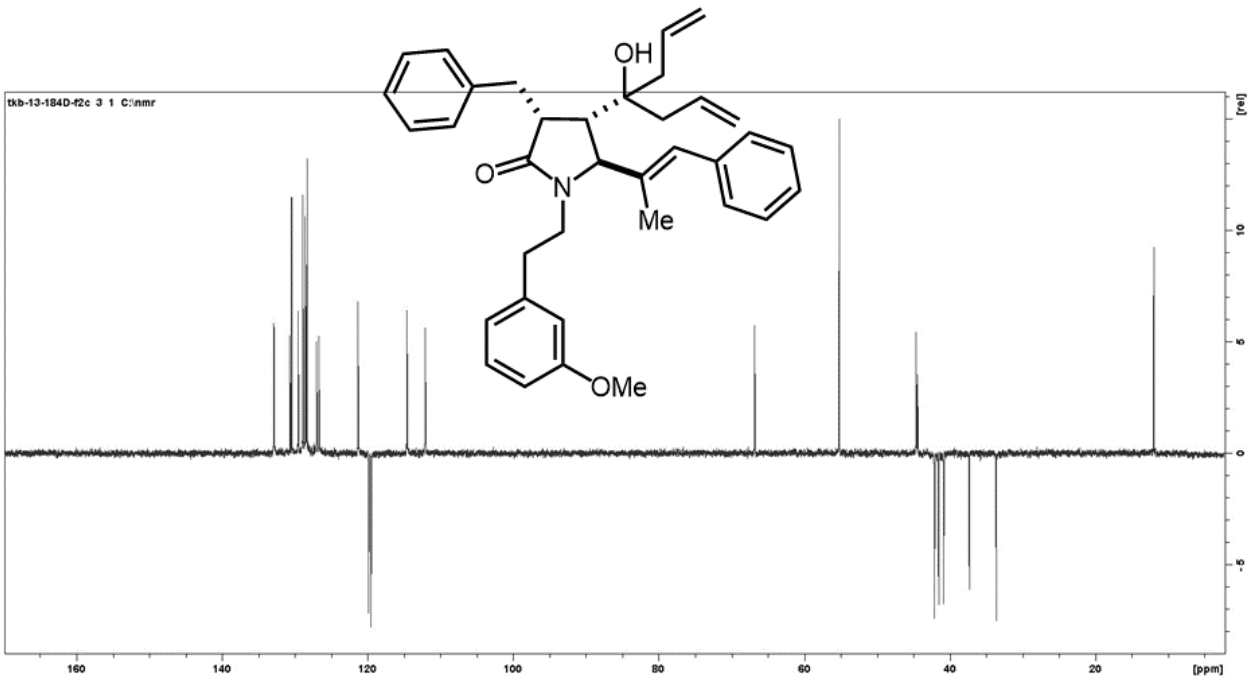
Prepared in 0.50 mmol scale using **General Procedures C** and **D**. Grignard reagent = allylmagnesium bromide and electrophile = benzyl bromide. Purification: Flash chromatography on silica eluting with hexane/acetone (95:5 to 50:50). Yellowish oil. Yield = 227.7 mg, 85%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14 – 6.94 (m, 11H), 6.62 – 6.52 (m, 3H), 6.11 (s, 1H), 5.58 (ddt, *J* = 17.3, 10.3, 7.2 Hz, 1H), 5.37 (ddt, *J* = 17.4, 10.2, 7.3 Hz, 1H), 5.00 (dd, *J* = 10.2, 2.1 Hz, 1H), 4.97 – 4.84 (m, 2H), 4.87 – 4.76 (m, 1H), 3.74 (dd, *J* = 17.9, 5.3 Hz, 1H), 3.73 – 3.56 (m, 1H), 3.57 (s, 3H), 3.08 (dd, *J* = 13.5, 5.9 Hz, 1H), 2.83 (dd, *J* = 13.4, 5.3 Hz, 1H), 2.72 (dqd, *J* = 13.2, 6.4, 3.2 Hz, 3H), 2.58 (ddt, *J* = 11.9, 9.0, 6.3 Hz, 1H), 2.04 – 1.92 (m, 4H), 1.55 (s, 1H), 0.93 (d, *J* = 1.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.23, 159.78, 140.72, 138.62, 136.82, 136.51, 132.89, 132.79, 130.63, 130.39, 129.48, 128.85, 128.52, 128.28, 126.97, 126.66, 121.27, 119.78,

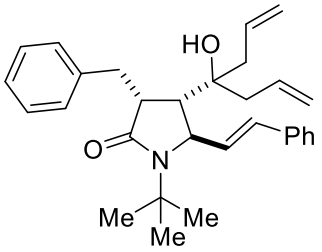
119.46, 114.53, 112.04, 74.66, 66.78, 55.14, 44.60, 44.44, 42.07, 41.50, 40.81, 37.30, 33.58, 11.95.

HRMS-EI^{+} (*m/z*): calc for $C_{36}H_{41}NO_3$ $[M]^{+}$ 535.3086, found 535.3093.







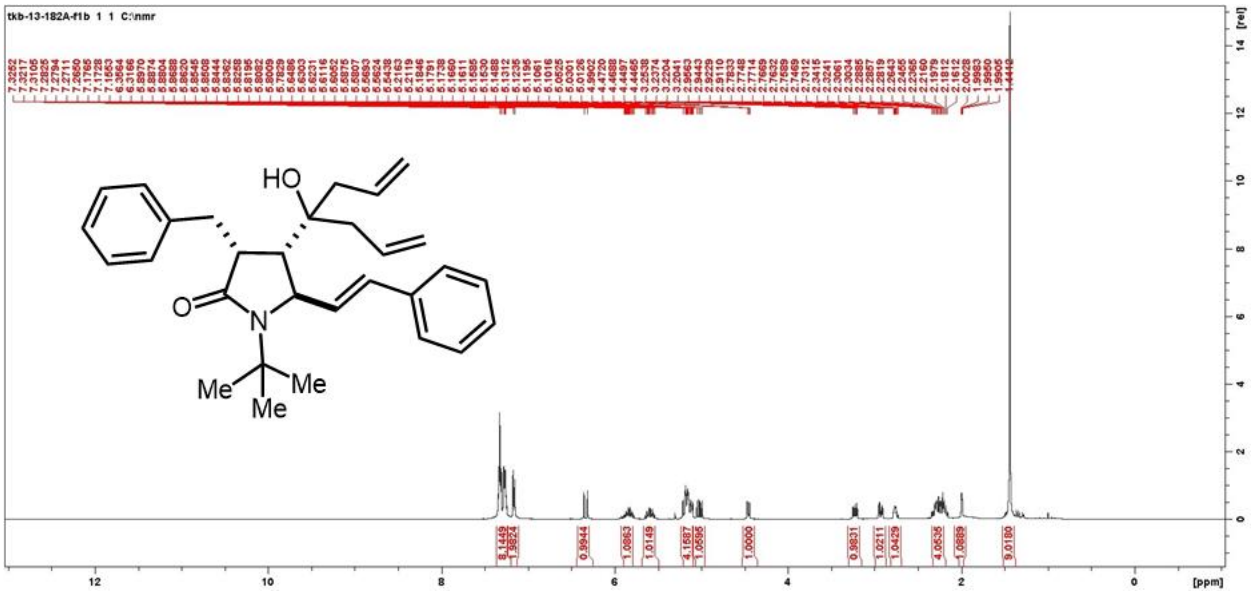


8l; 92%, >99:1 dr

E^+ = benzyl bromide

Compound 8l

Prepared in 0.50 mmol scale using **General Procedures C** and **D**. Grignard reagent = allylmagnesium bromide and electrophile = benzyl bromide. Purification: Flash chromatography on silica eluting with hexane/acetone (95:5 to 70:30). Yellowish oil. Yield = 204.1 mg, 92%, >99:1 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.26 (m, 8H), 7.18 – 7.15 (m, 2H), 6.34 (d, *J* = 16.0 Hz, 1H), 5.86 (dddt, *J* = 21.3, 17.3, 10.2, 7.3 Hz, 1H), 5.60 (ddt, *J* = 17.5, 10.2, 7.3 Hz, 1H), 5.24 – 5.09 (m, 4H), 5.02 (dd, *J* = 16.0, 9.0 Hz, 1H), 4.46 (dd, *J* = 9.0, 1.9 Hz, 1H), 3.23 (dd, *J* = 13.3, 6.5 Hz, 1H), 2.93 (dd, *J* = 13.3, 4.8 Hz, 1H), 2.81 – 2.71 (m, 1H), 2.37 – 2.14 (m, 4H), 2.00 (dd, *J* = 3.3, 1.8 Hz, 1H), 1.44 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.59, 138.81, 136.37, 133.83, 132.97, 132.92, 130.41, 129.87, 128.57, 128.46, 127.69, 126.86, 126.50, 119.91, 119.64, 76.76, 75.11, 61.16, 55.30, 48.84, 46.67, 40.74, 39.88, 37.47, 28.30. **HRMS-EI$^+$** (*m/z*): calc for $C_{30}H_{37}NO_2$ $[M]^+$ 443.2824, found 443.2828.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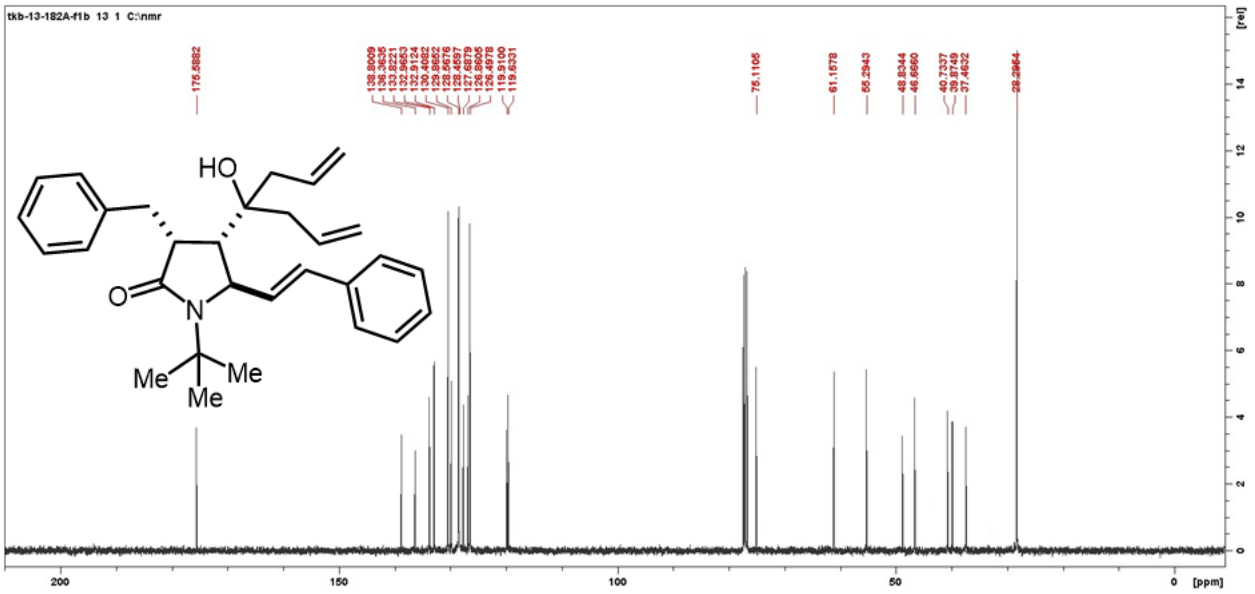
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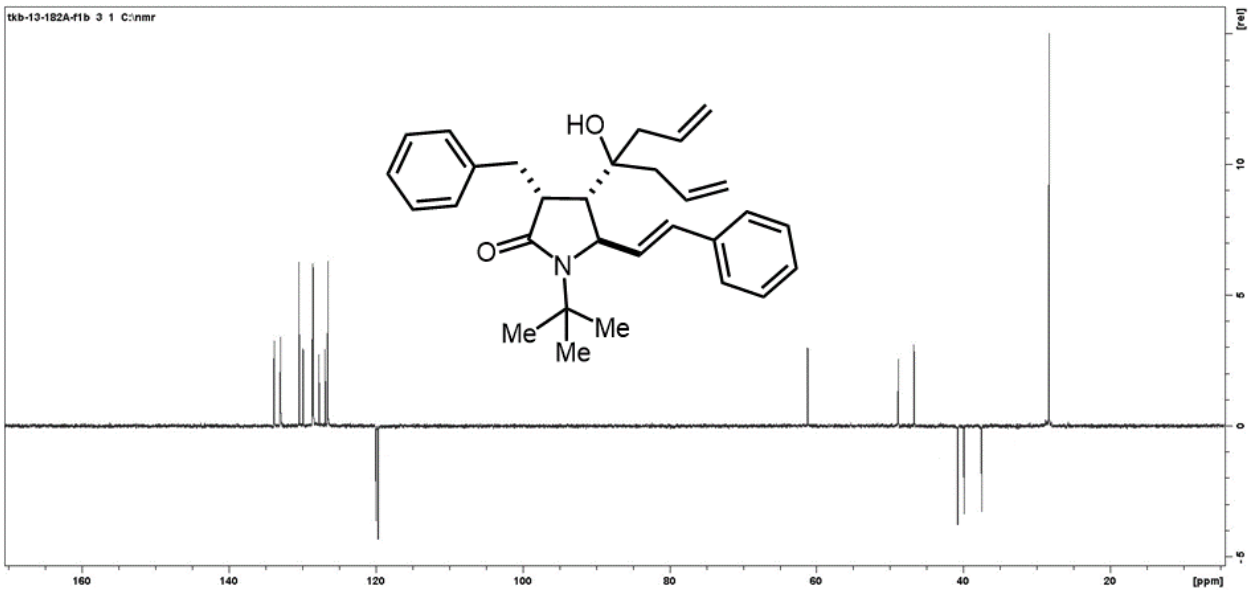
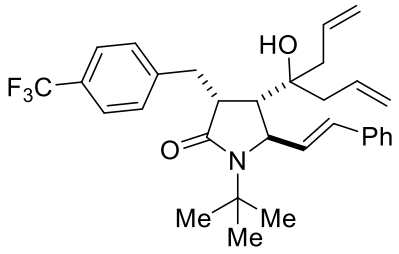
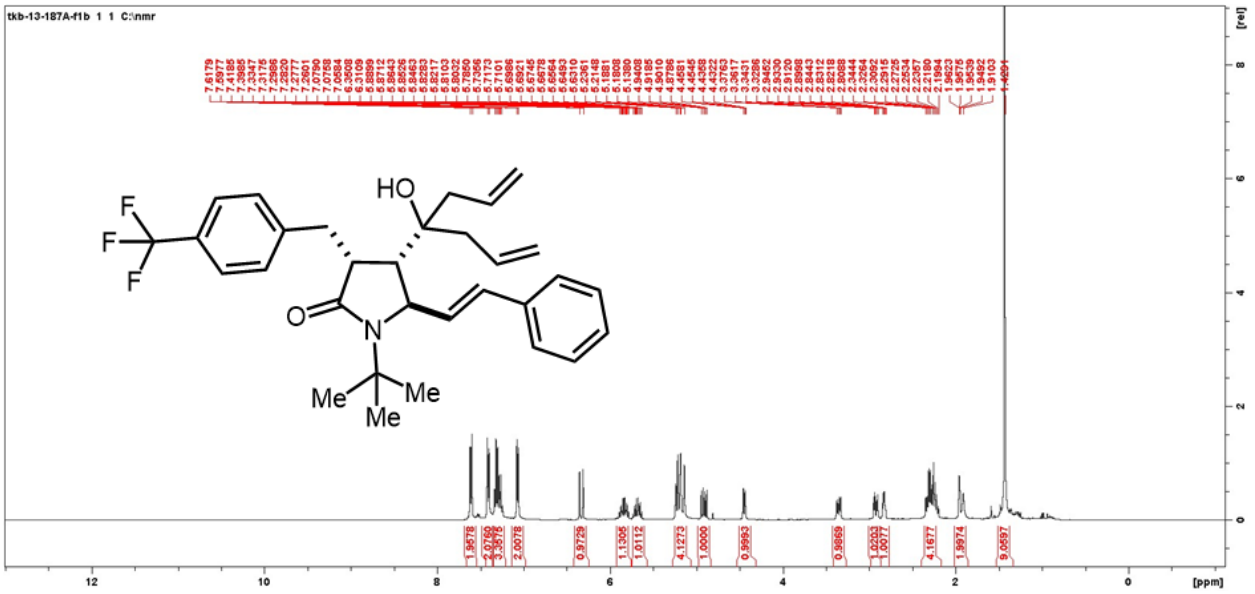




8m; 82%, >99:1 dr

Compound 8m

Prepared in 0.50 mmol scale using **General Procedures C** and **D**. Grignard reagent = allylmagnesium bromide and electrophile = 4-trifluoromethylbenzyl bromide. Purification: Flash chromatography on silica eluting with hexane/acetone (95:5 to 70:30). Yellowish oil. Yield = 209.8 mg, 82%, >99:1 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, *J* = 8.0 Hz, 2H), 7.44 – 7.22 (m, 5H), 7.10 – 7.03 (m, 2H), 6.33 (d, *J* = 16.0 Hz, 1H), 5.84 (ddt, *J* = 17.3, 10.2, 7.3 Hz, 1H), 5.68 (ddt, *J* = 17.4, 10.2, 7.3 Hz, 1H), 5.26 – 5.15 (m, 4H), 4.91 (dd, *J* = 15.9, 8.9 Hz, 1H), 4.45 (dd, *J* = 9.0, 2.0 Hz, 1H), 3.35 (dd, *J* = 13.3, 5.8 Hz, 1H), 2.92 (dd, *J* = 13.3, 4.9 Hz, 1H), 2.83 (td, *J* = 5.4, 3.5 Hz, 1H), 2.37 – 2.18 (m, 4H), 1.96-1.91 (m, 2H), 1.43 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.07, 143.05, 135.97, 133.08, 132.71, 130.84, 130.31, 128.67, 127.92, 126.18, 125.42, 125.38, 125.35, 125.31, 122.96, 120.07, 119.97, 118.72, 76.74, 75.15, 61.06, 55.45, 48.66, 46.10, 40.79, 40.05, 37.05, 28.27. **HRMS-EI^{+}** (*m/z*): calc for $C_{31}H_{36}F_3NO_2$ $[M]^{+}$ 511.2698, found 511.2694.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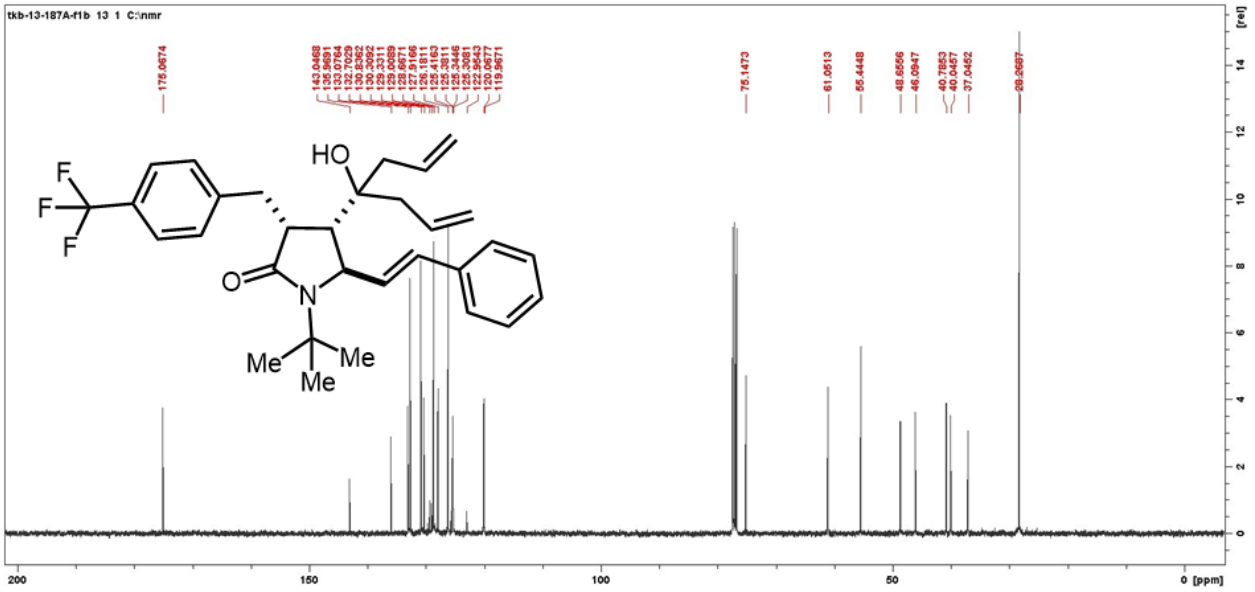
[ppm]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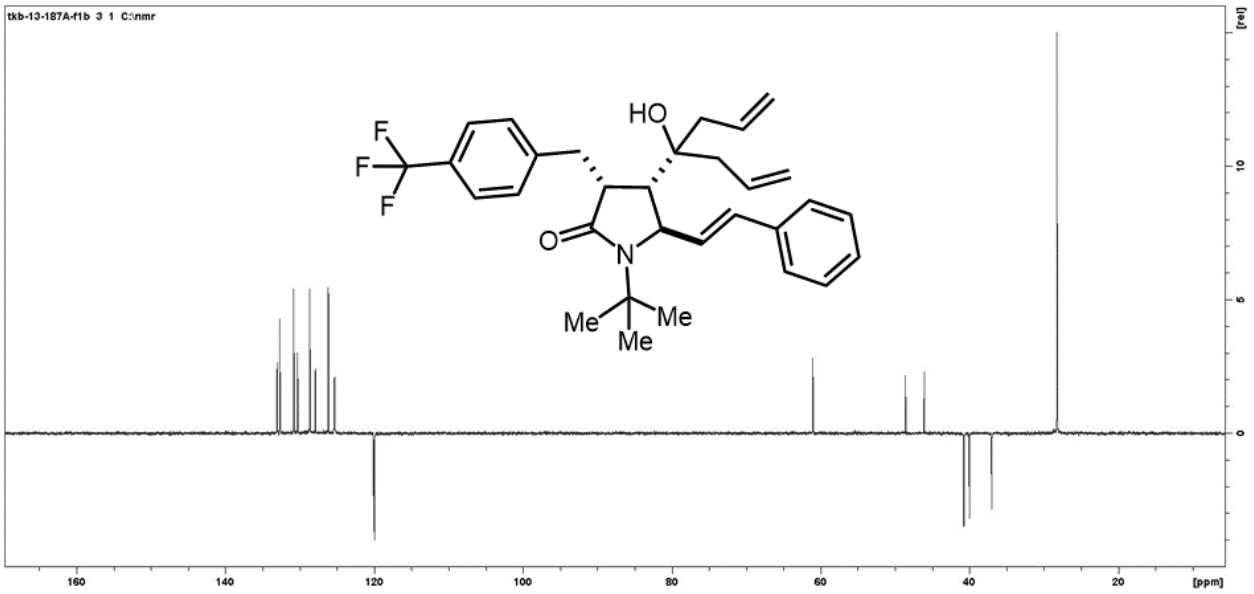
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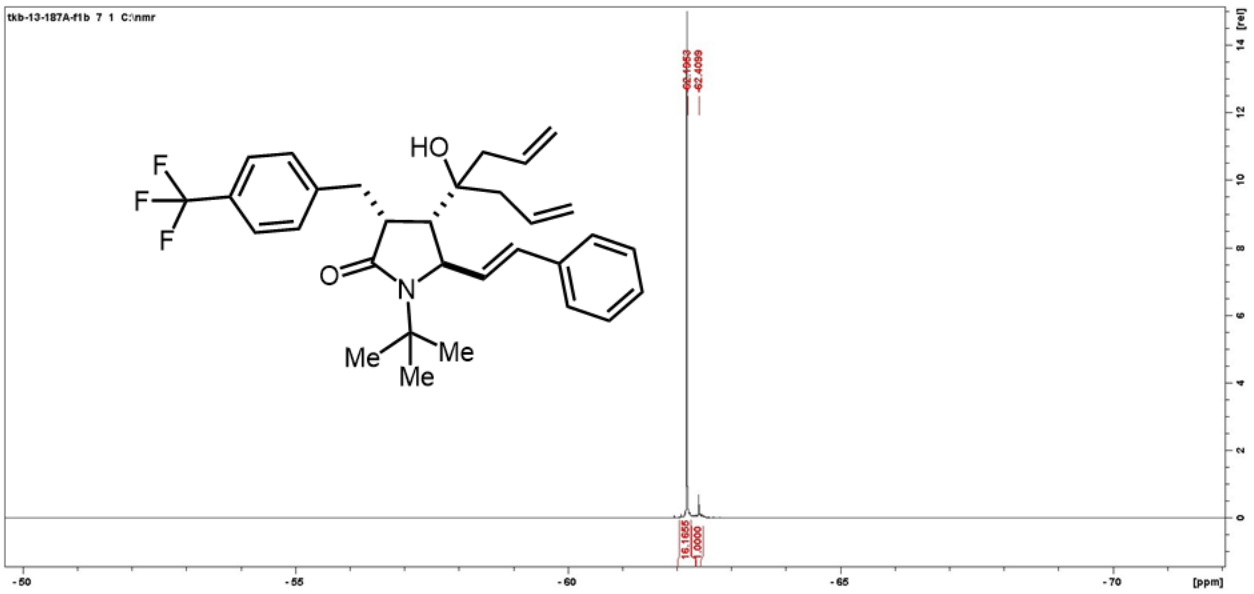
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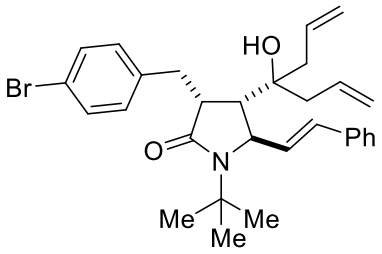
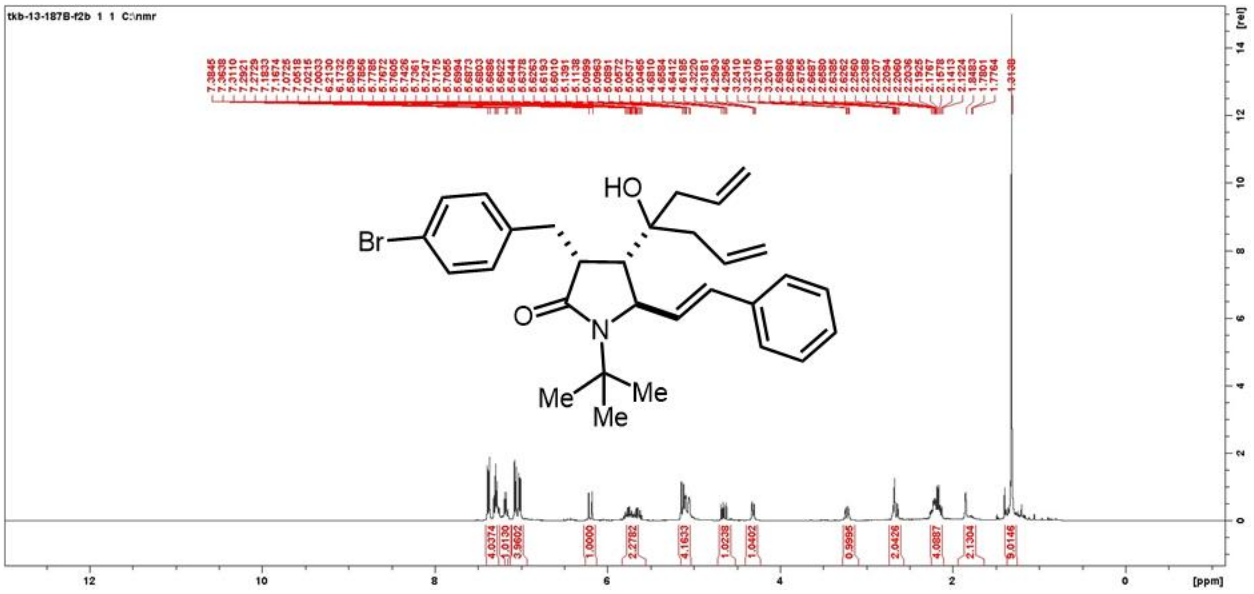
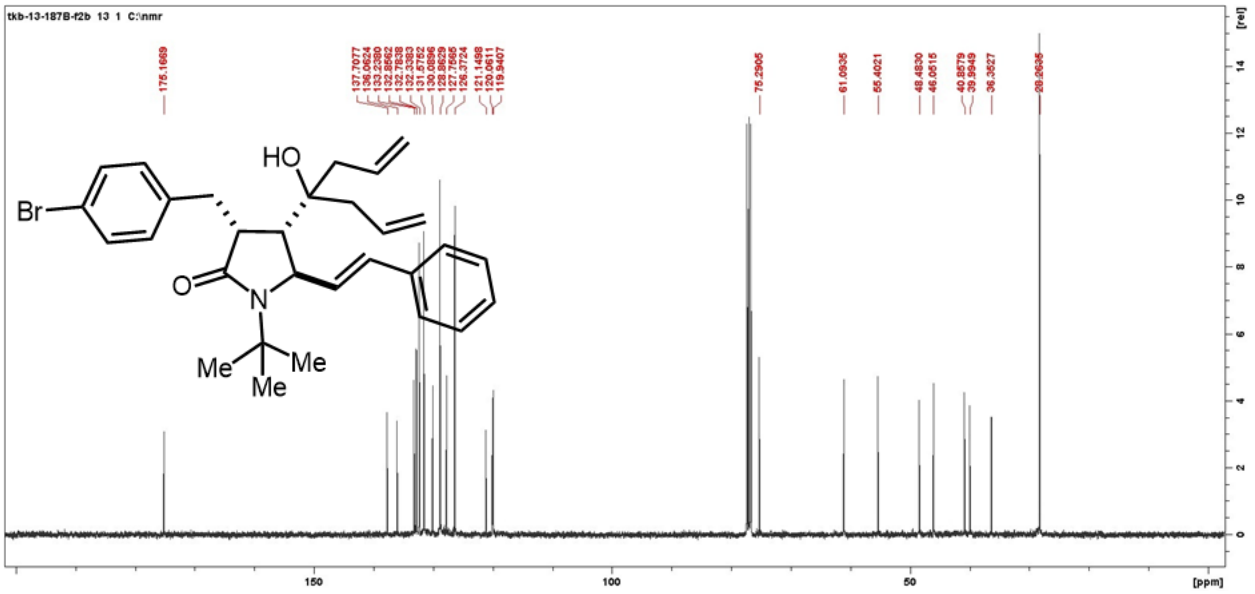


8n; 85%, >99:1 dr

Compound 8n

Prepared in 0.50 mmol scale using **General Procedures C** and **D**. Grignard reagent = allylmagnesium bromide and electrophile = 4-bromobenzyl bromide. Purification: Flash chromatography on silica eluting with hexane/acetone (95:5 to 70:30). Yellowish oil. Yield = 222.1 mg, 85%, >99:1 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.33 (m, 2H), 7.28 (q, *J* = 8.0 Hz, 3H), 7.17 (td, *J* = 7.2, 1.4 Hz, 1H), 7.04 (ddd, *J* = 20.3, 7.2, 1.6 Hz, 3H), 6.19 (d, *J* = 15.9 Hz, 1H), 5.70 (dddt, *J* = 39.3, 17.4, 10.2, 7.3 Hz, 2H), 5.17 – 4.98 (m, 4H), 4.65 (dd, *J* = 15.9, 9.1 Hz, 1H), 4.31 (dd, *J* = 9.1, 2.0 Hz, 1H), 3.28 – 3.17 (m, 1H), 2.72 – 2.60 (m, 2H), 2.35 – 2.10 (m, 4H), 1.85 (dd, *J* = 3.2, 1.9 Hz, 1H), 1.31 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.17, 137.71, 136.07, 133.24, 132.86, 132.79, 132.34, 131.58, 130.09, 128.87, 127.76, 126.38, 121.15, 120.07, 119.94, 76.73, 75.29, 61.10, 55.41, 48.49, 46.06, 40.86, 40.00, 36.36, 28.27. **HRMS-EI^{+}** (*m/z*): calc for $C_{30}H_{36}BrNO_2$ $[M]^+$ 521.1929, found 521.1933.

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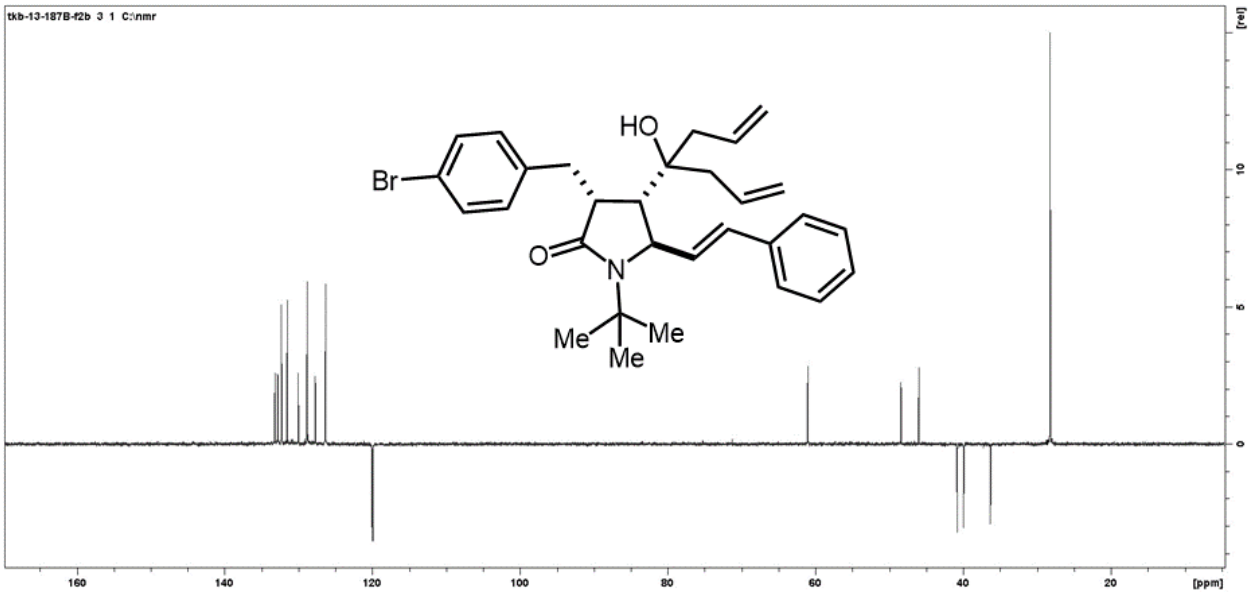
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N
Me
Me
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[rel]
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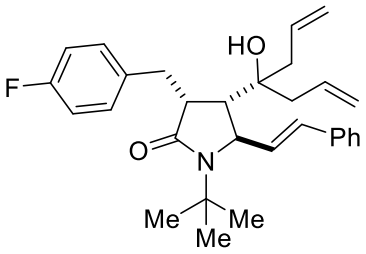
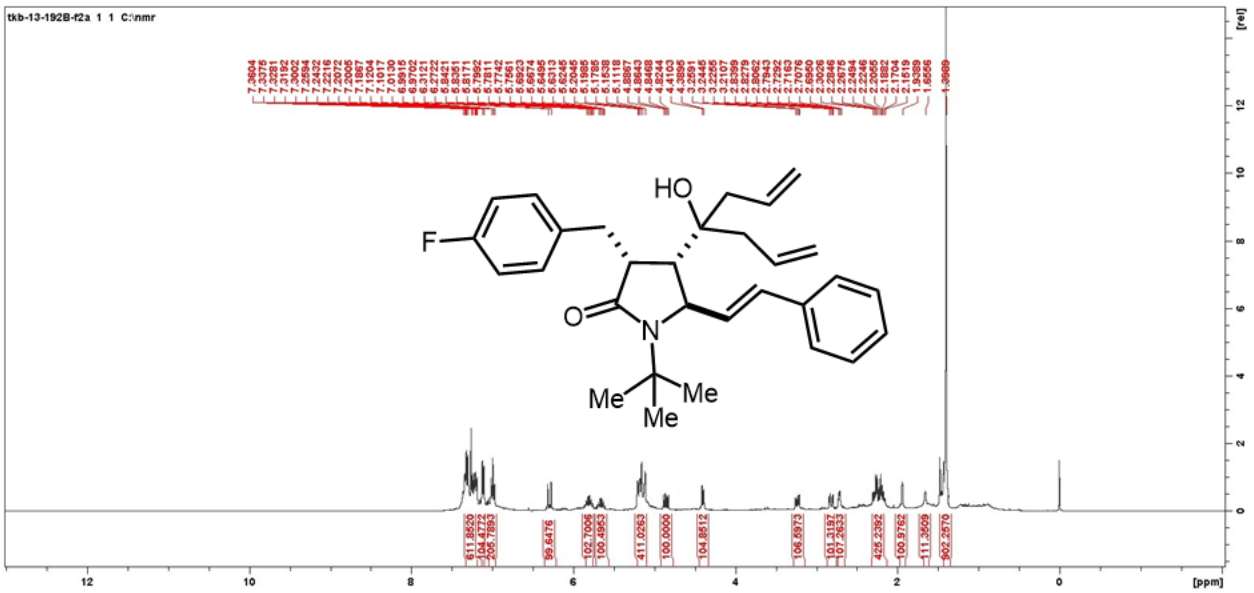
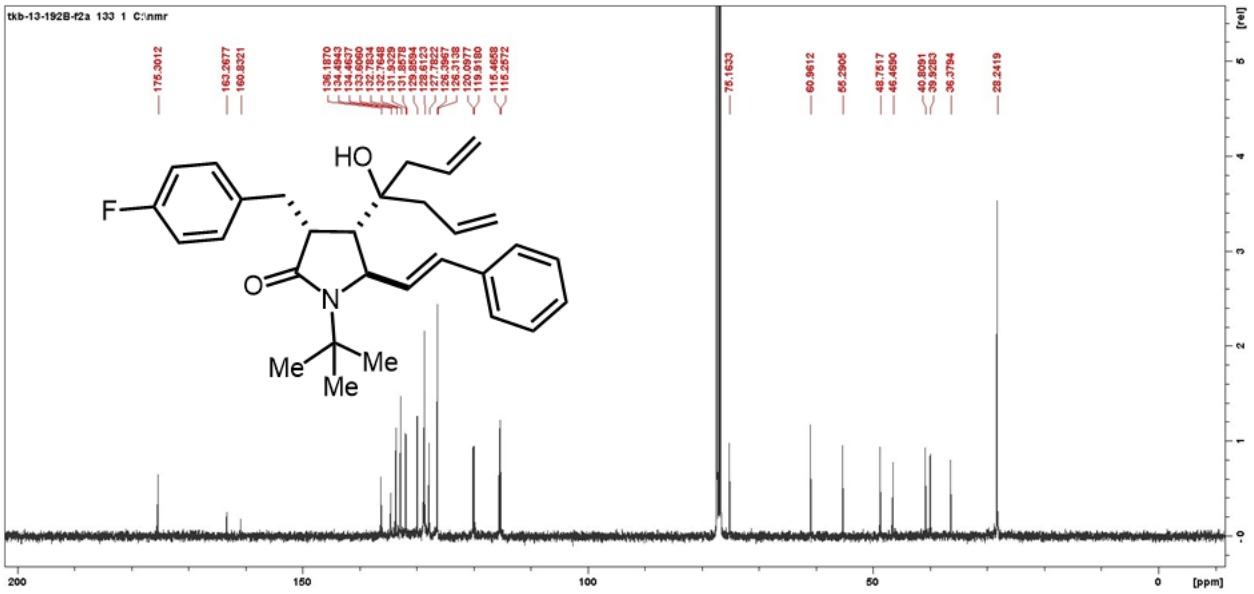


8o; 81%, >99:1 dr

Compound 8o

Prepared in 0.50 mmol scale using **General Procedures C** and **D**. Grignard reagent = allylmagnesium bromide and electrophile = 4-fluorobenzyl bromide. Purification: Flash chromatography on silica eluting with hexane/acetone (95:5 to 70:30). Yellowish oil. Yield = 186.9 mg, 81%, >99:1 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.21 (m, 5H), 7.20 (dd, *J* = 8.5, 5.7 Hz, 2H), 7.17 – 7.04 (m, 2H), 6.35 – 6.23 (m, 1H), 5.81 (ddt, *J* = 17.3, 10.1, 7.2 Hz, 1H), 5.66 (ddt, *J* = 17.4, 10.2, 7.3 Hz, 1H), 5.17 – 5.06 (m, 4H), 4.86 (dd, *J* = 15.9, 8.9 Hz, 1H), 4.40 (dd, *J* = 8.9, 1.9 Hz, 1H), 3.24 (dd, *J* = 13.6, 5.9 Hz, 1H), 2.82 (dd, *J* = 13.5, 4.8 Hz, 1H), 2.71 (td, *J* = 5.3, 3.3 Hz, 1H), 2.23 (dtd, *J* = 21.5, 14.4, 7.3 Hz, 4H), 1.94 (dd, *J* = 3.3, 1.8 Hz, 1H), 1.66 (s, 1H), 1.40 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.31, 163.27, 160.84, 136.19, 134.50, 134.47, 133.61, 132.79, 132.77, 131.94, 131.86, 129.86, 128.87, 128.78, 128.62, 128.46, 127.79, 126.49, 126.40, 126.32, 120.10, 119.92, 115.47, 115.26, 76.70, 75.17, 60.96, 55.29, 48.76, 46.47, 40.81, 39.93, 28.25. **HRMS-EI**$^{+}$ (*m/z*): calc for $C_{30}H_{36}FNO_2$ $[M]^{+}$ 461.2730, found 461.2738.

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55.2905
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39.9283
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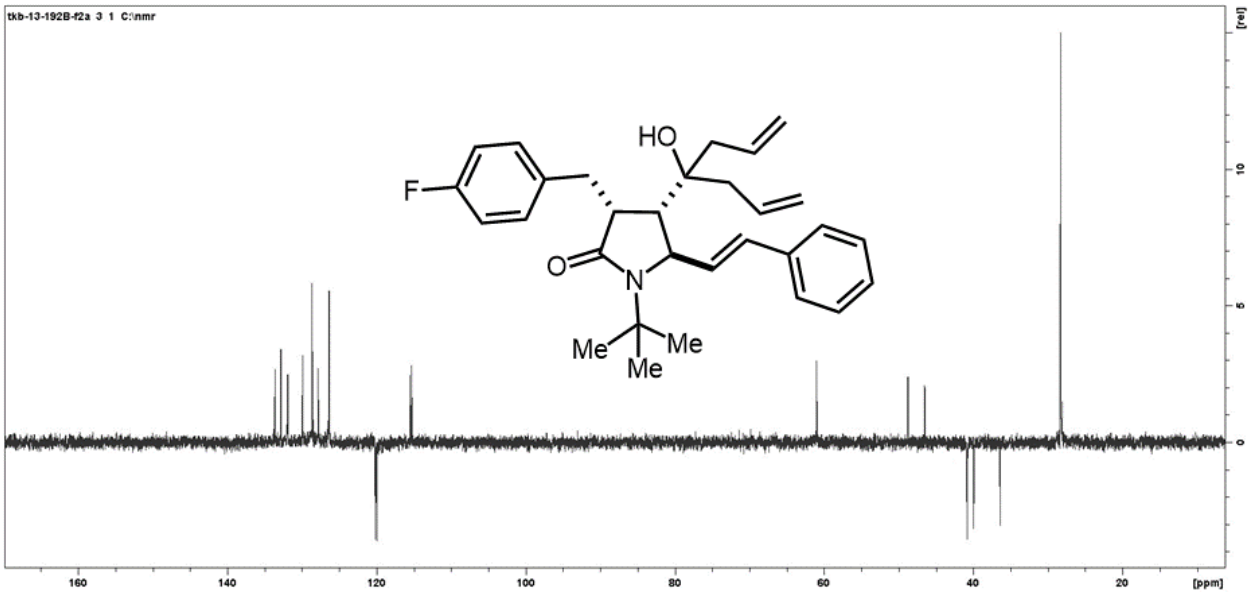
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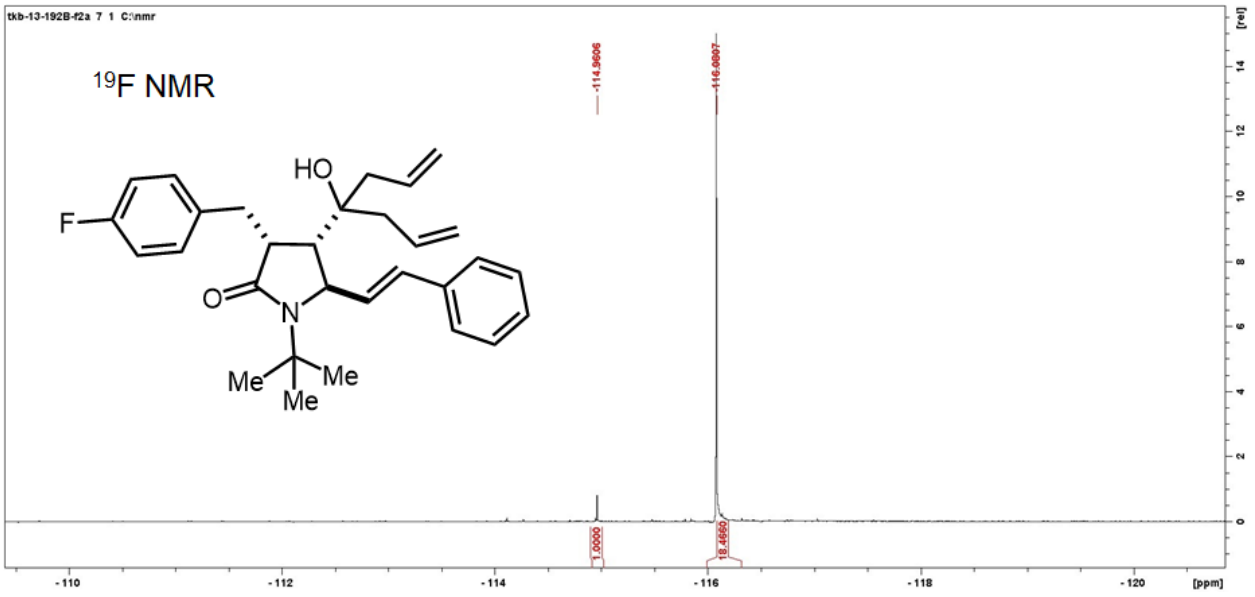
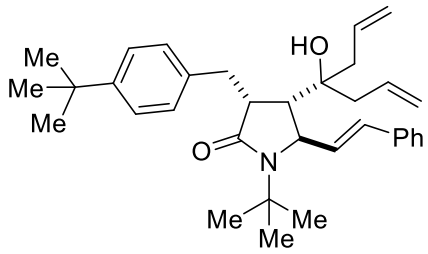
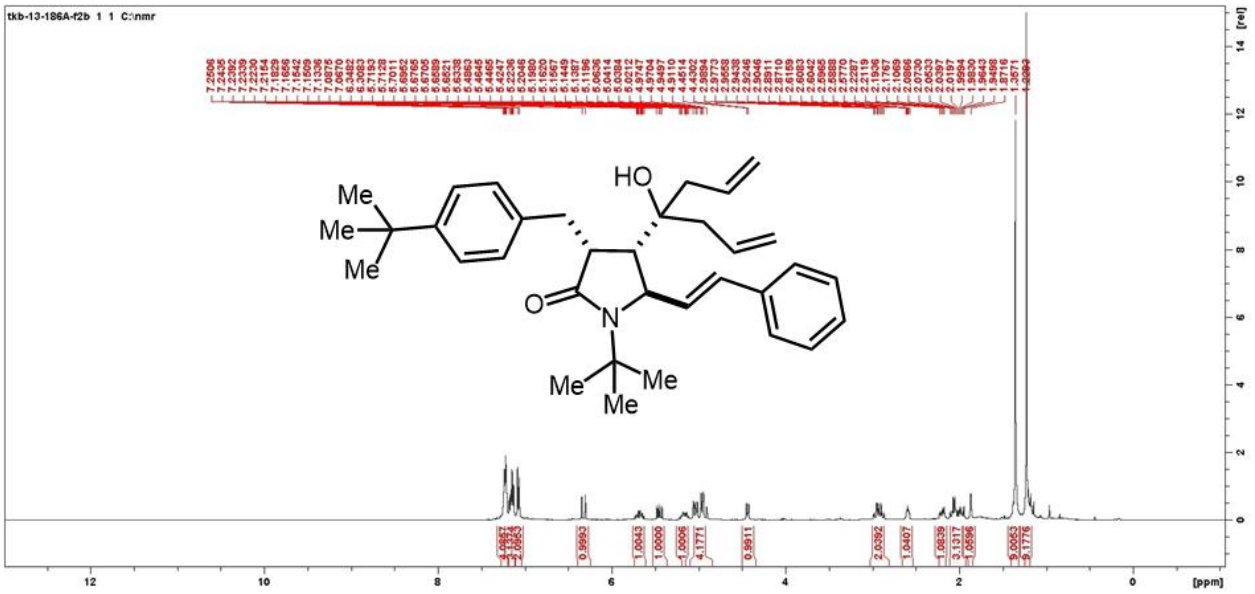




8p; 87%, >99:1 dr

Compound 8p

Prepared in 0.50 mmol scale using **General Procedures C** and **D**. Grignard reagent = allylmagnesium bromide and electrophile = 4-*tert*-butylbenzyl bromide. Purification: Flash chromatography on silica eluting with hexane/acetone (95:5 to 80:20). Yellowish oil. Yield = 217.4 mg, 87%, >99:1 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 – 7.01 (m, 9H), 6.33 (d, *J* = 15.9 Hz, 1H), 5.76 – 5.61 (m, 1H), 5.46 (dd, *J* = 15.9, 8.7 Hz, 1H), 5.25 – 5.10 (m, 1H), 5.09 – 4.88 (m, 4H), 4.44 (dd, *J* = 8.8, 1.8 Hz, 1H), 2.93 (qd, *J* = 13.4, 6.4 Hz, 2H), 2.60 (ddd, *J* = 8.0, 4.9, 2.9 Hz, 1H), 2.19 (dt, *J* = 15.9, 7.8 Hz, 1H), 2.13 – 1.92 (m, 3H), 1.87 (dd, *J* = 2.9, 1.7 Hz, 1H), 1.36 (s, 9H), 1.23 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.78, 149.65, 136.48, 135.71, 133.93, 133.07, 132.85, 130.18, 129.84, 128.69, 127.77, 126.37, 125.43, 119.89, 119.37, 74.86, 61.28, 55.27, 49.32, 47.06, 40.56, 39.75, 37.53, 31.43, 28.37. **HRMS-EI^{+}** (*m/z*): calc for $C_{34}H_{45}NO_2$ $[M]^{+}$ 499.3450, found 499.3457.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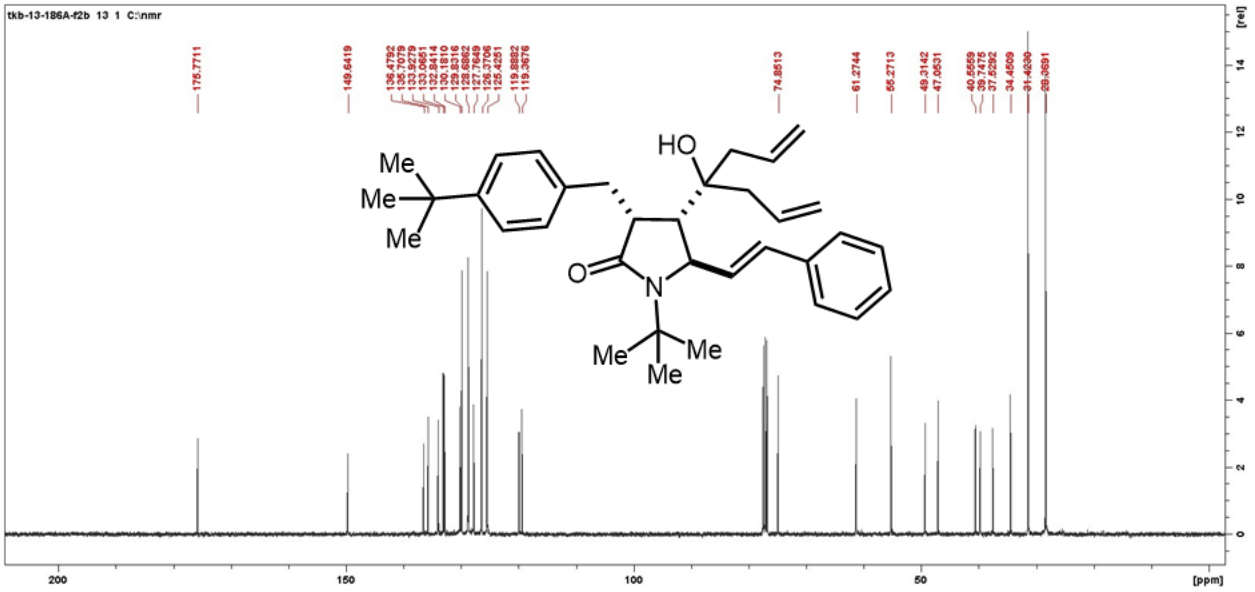
Me
O
N
Me
Me
Me
[rel]
[ppm]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133.9570
133.0651
132.8414
130.1810
128.8916
128.6862
127.7649
126.3706
125.4251
119.8882
119.3676
74.8513
61.2744
55.2713
49.3142
47.0531
40.5559
39.7475
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Me
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O
N
Me
Me
Me
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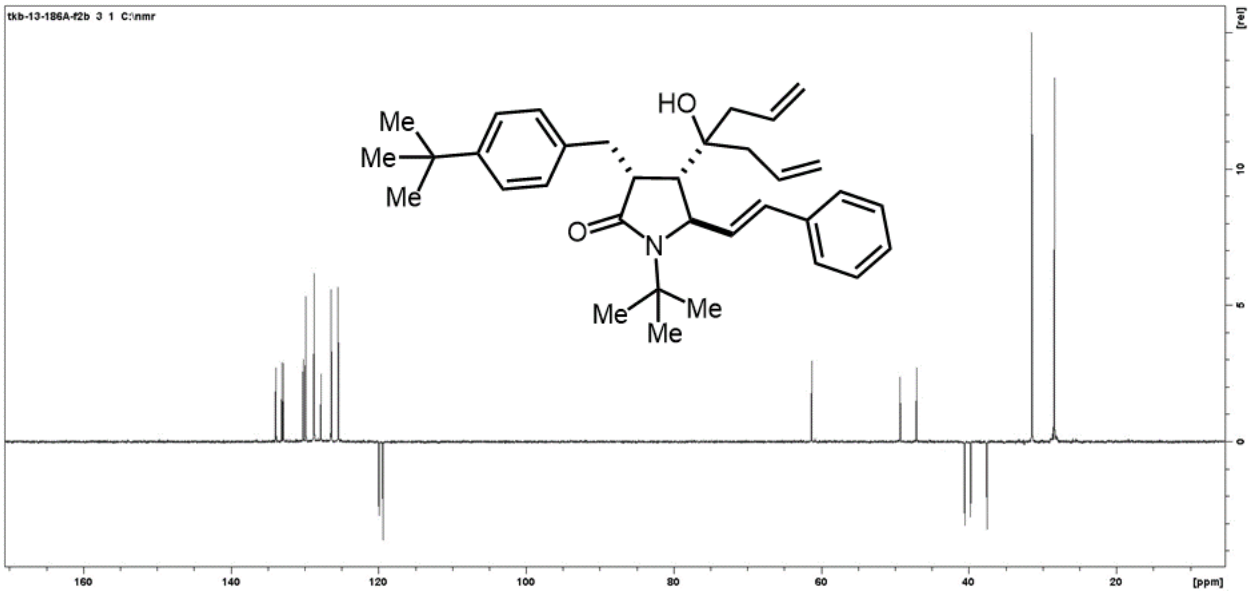
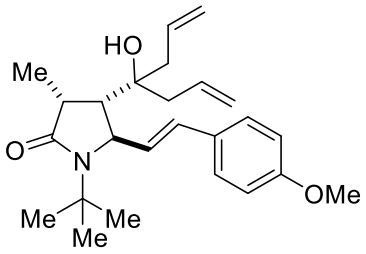
[ppm]

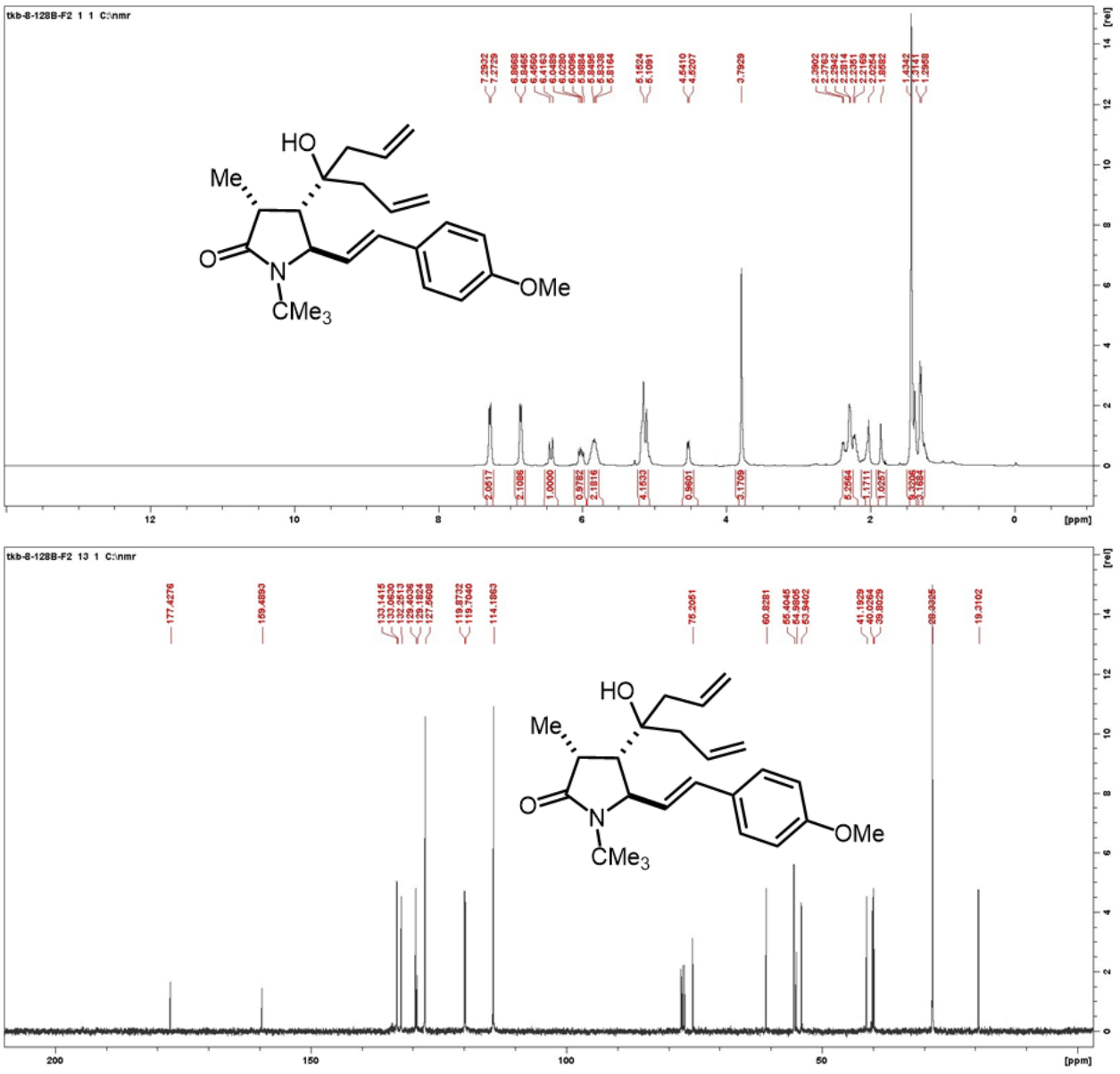




8q; 89%, 95:5 dr
E^+ = MeI

Compound 8q

Prepared in 0.50 mmol scale using **General Procedures C** and **D**. Grignard reagent = allylmagnesium bromide and electrophile = methyl iodide. Purification: Flash chromatography on silica eluting with hexane/acetone (95:5 to 70:30). Yellowish oil. Yield = 176.9 mg, 89%, 95:5 dr. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.28 (d, *J* = 8.1 Hz, 2H), 6.86 (d, *J* = 8.1 Hz, 2H), 6.44 (d, *J* = 15.9 Hz, 1H), 6.02 (dd, *J* = 16.0, 8.4 Hz, 1H), 5.84 (tdd, *J* = 21.3, 10.3, 4.9 Hz, 2H), 5.15 – 5.11 (m, 4H), 4.53 (d, *J* = 8.4 Hz, 1H), 3.79 (s, 3H), 2.32 – 2.16 (m, 5H), 2.04 (d, *J* = 8.5 Hz, 1H), 1.86 (s, 1H), 1.43 (s, 9H), 1.31 (d, *J* = 7.7 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.43, 159.49, 133.15, 133.07, 132.26, 129.41, 127.56, 119.88, 119.71, 114.19, 75.21, 60.83, 55.41, 54.98, 53.94, 41.20, 40.03, 39.81, 28.34, 19.31. **HRMS-EI$^+$** (*m/z*): calc for $C_{25}H_{35}NO_3$ $[M]^+$ 397.2617, found 397.2623.


tkb-8-128B-F2 1 1 C6nmr
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O
N
CMe3
OMe
[ppm]
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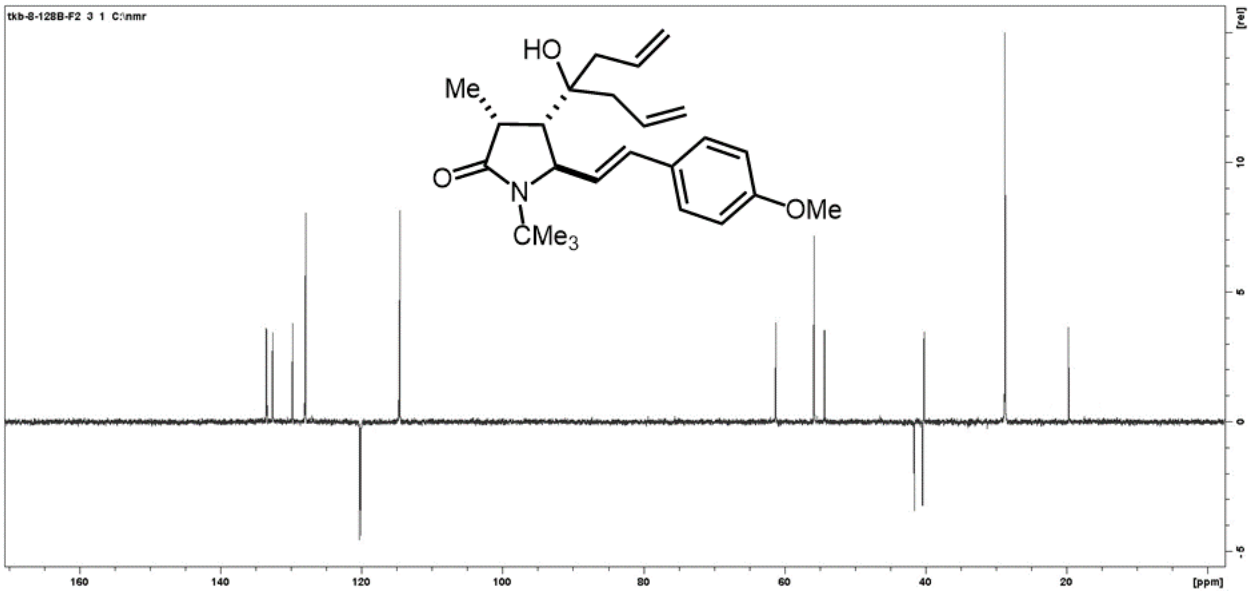
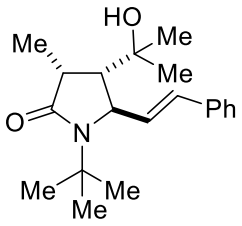
Me
O
N
CMe3
OMe
[ppm]



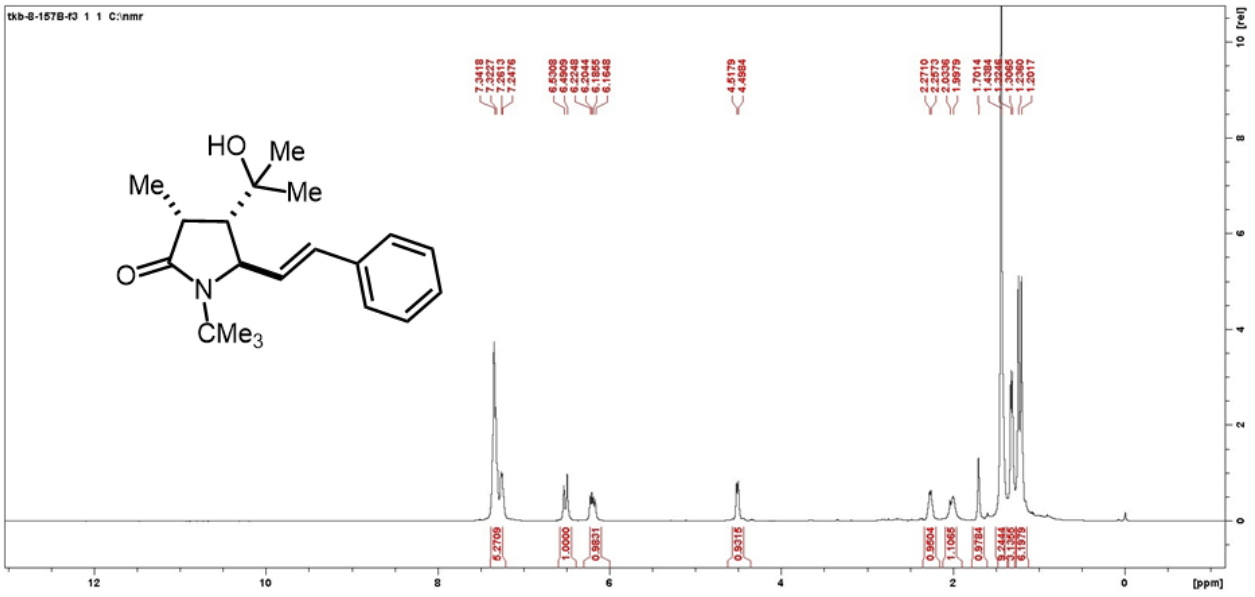


8r; 86%, 95:5 dr

E^+ = MeI

Compound 8r

Prepared in 0.50 mmol scale using **General Procedures C** and **D**. Grignard reagent = methylmagnesium bromide and electrophile = methyl iodide. Purification: Flash chromatography on silica eluting with hexane/acetone (95:5 to 80:20). Yellowish oil. Yield = 135.6 mg, 86%, 95:5 dr. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.34 - 7.25 (m, 5H), 6.51 (d, *J* = 16.0 Hz, 1H), 6.20 (dd, *J* = 15.9, 8.3 Hz, 1H), 4.51 (d, *J* = 8.2 Hz, 1H), 2.26 (tt, *J* = 7.8, 4.8 Hz, 1H), 2.00 (br s, 1H), 1.70 (s, 1H), 1.44 (s, 9H), 1.32 (d, *J* = 7.5 Hz, 3H), 1.22 (s, 3H), 1.14 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.50, 136.51, 134.95, 129.67, 128.76, 127.88, 126.37, 72.66, 61.20, 57.60, 54.97, 40.61, 28.34, 27.72, 25.04, 19.65. **HRMS-EI$^+$** (*m/z*): calc for $C_{20}H_{29}NO_2$ $[M]^+$ 315.2198, found 315.2193.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O
N
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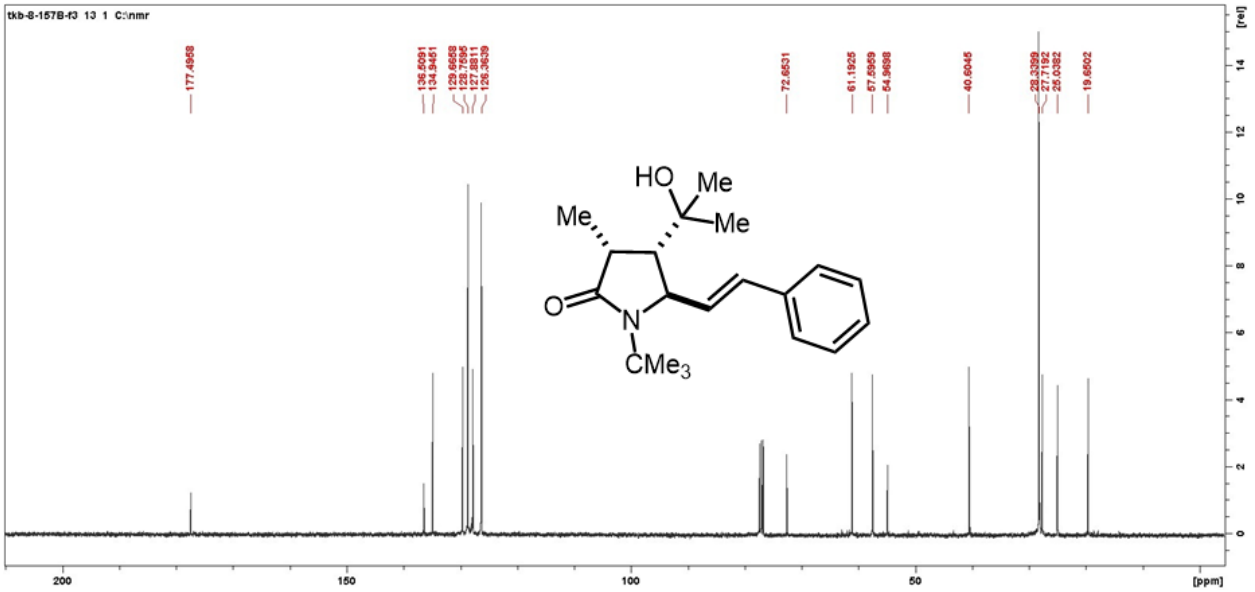
[ppm]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129.6658
128.7595
127.8811
126.3639
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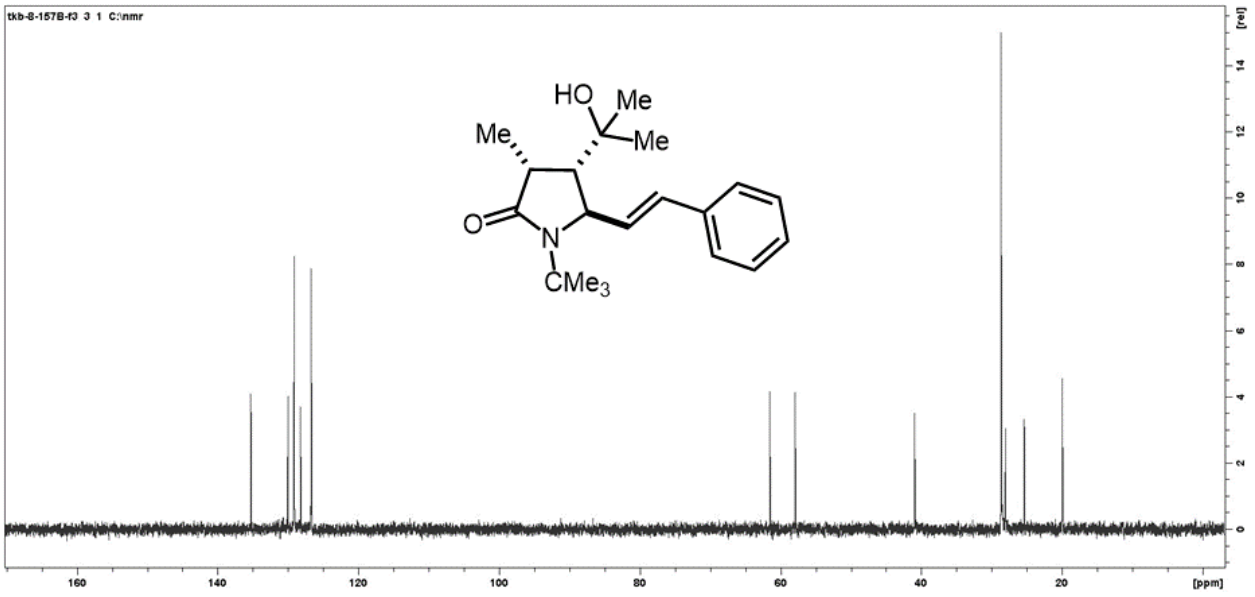
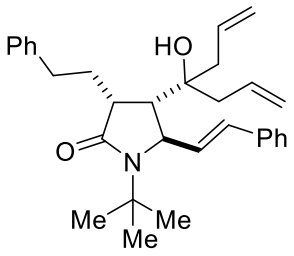
61.1925
57.5959
54.9698
40.6045
28.3369
27.7192
25.0382
19.6502
HO
Me
Me
Me
O
N
CMe3
[ppm]

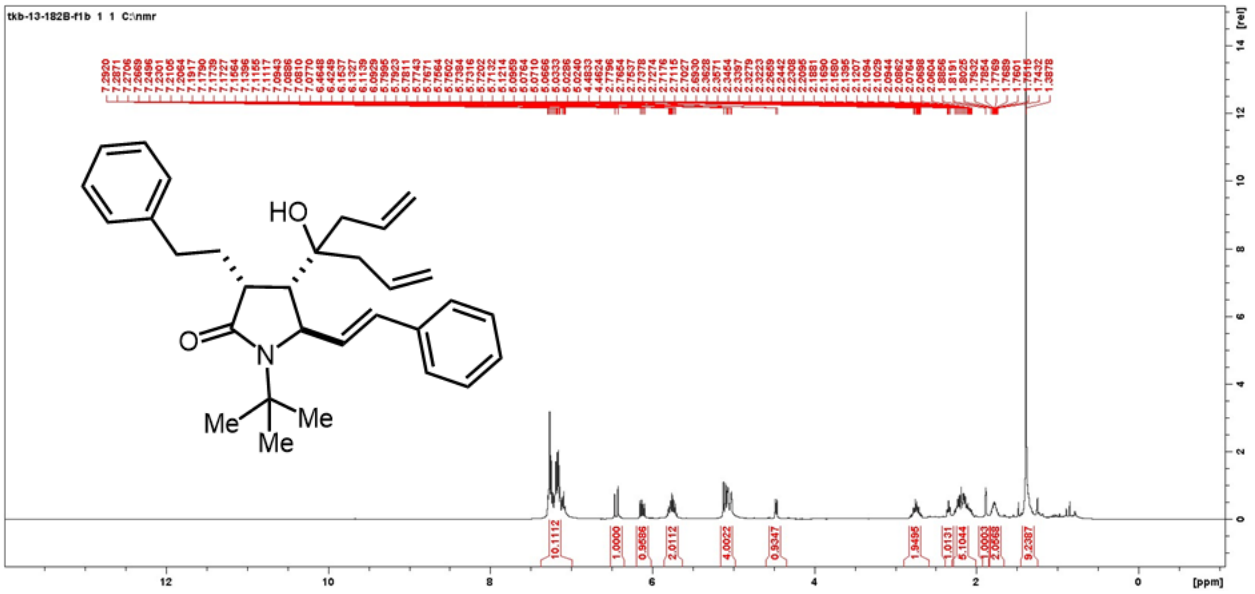




8s; 71%, >99:1 dr
E^+ = $PhCH_2CH_2Br$

Compound 8s

Prepared in 0.50 mmol scale using **General Procedures C** and **D**. Grignard reagent = allylmagnesium bromide and electrophile = phenethyl bromide. Purification: Flash chromatography on silica eluting with hexane/acetone (95:5 to 80:20). Yellowish oil. Yield = 162.4 mg, 71%, >99:1 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.04 (m, 10H), 6.45 (d, *J* = 15.9 Hz, 1H), 6.12 (dd, *J* = 15.9, 8.4 Hz, 1H), 5.78 – 5.71 (m, 2H), 5.12 – 5.02 (m, 4H), 4.47 (d, *J* = 8.4 Hz, 1H), 2.75 (pd, *J* = 13.7, 6.0 Hz, 2H), 2.34 (td, *J* = 7.0, 2.4 Hz, 1H), 2.30 – 2.02 (m, 5H), 1.89 (d, *J* = 3.7 Hz, 1H), 1.77 (ddt, *J* = 13.6, 10.1, 6.8 Hz, 2H), 1.39 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.63, 141.80, 136.39, 134.11, 132.89, 130.18, 128.74, 128.57, 128.39, 127.91, 126.37, 125.92, 120.03, 119.85, 74.98, 60.90, 55.05, 52.54, 44.24, 40.92, 40.26, 35.89, 33.86, 28.37. . **HRMS-EI$^+$** (*m/z*): calc for $C_{31}H_{39}NO_2$ $[M]^+$ 457.2981, found 457.2987.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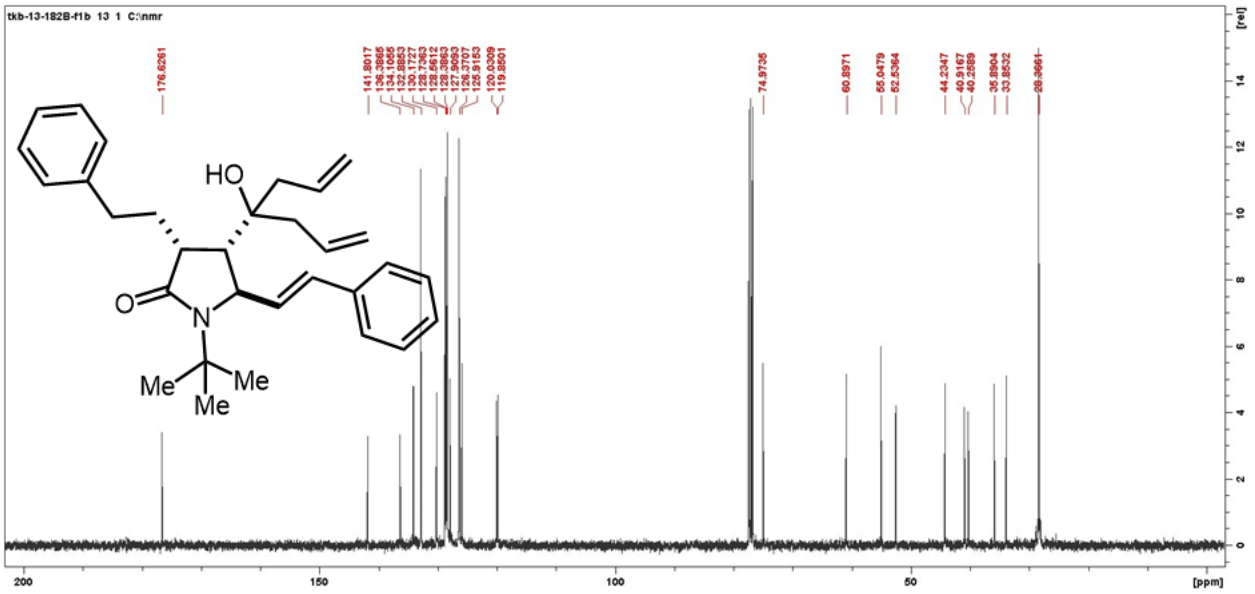
O
N
Me
Me
Me
[ppm]
[rel]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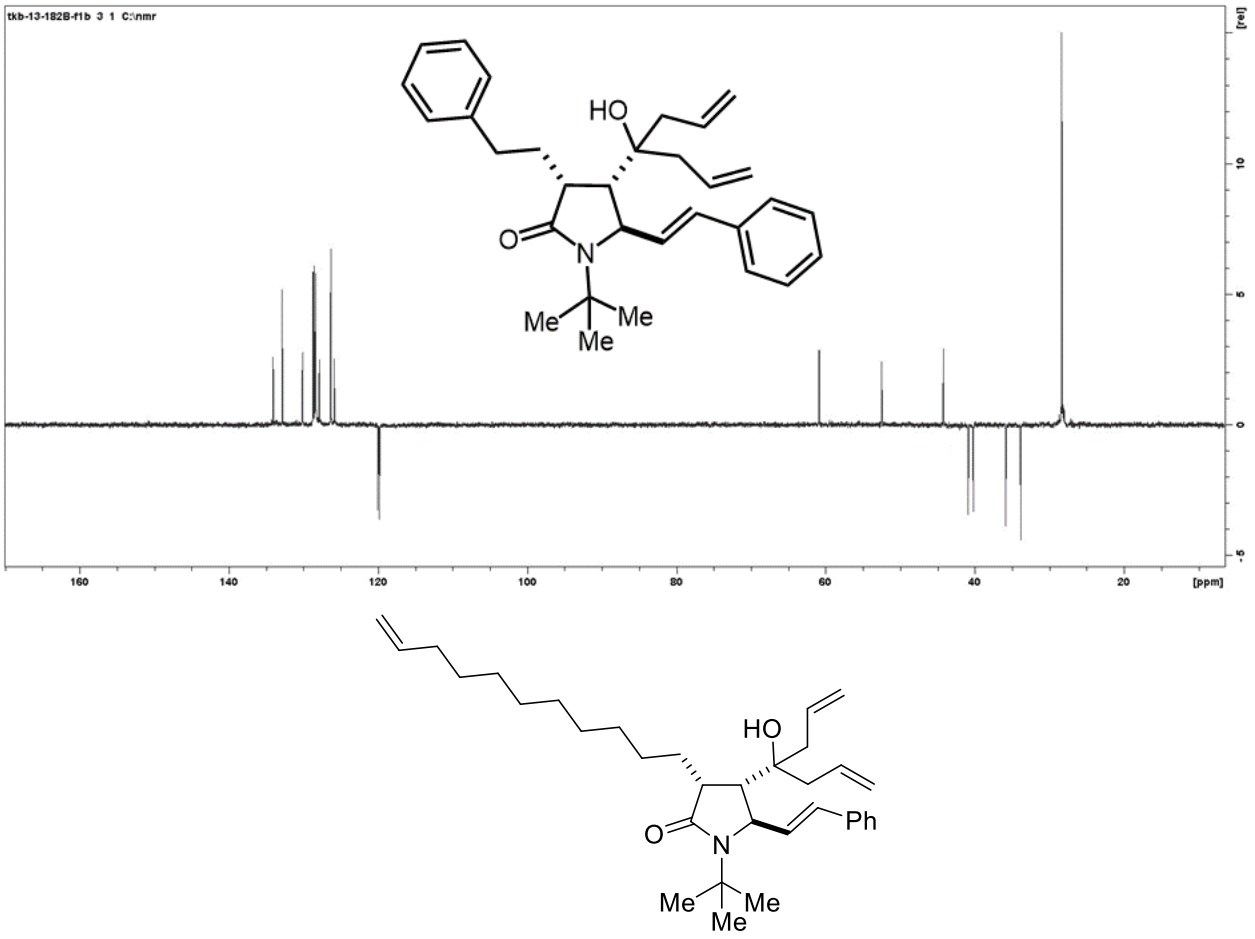
O
N
Me
Me
Me
[ppm]
[rel]

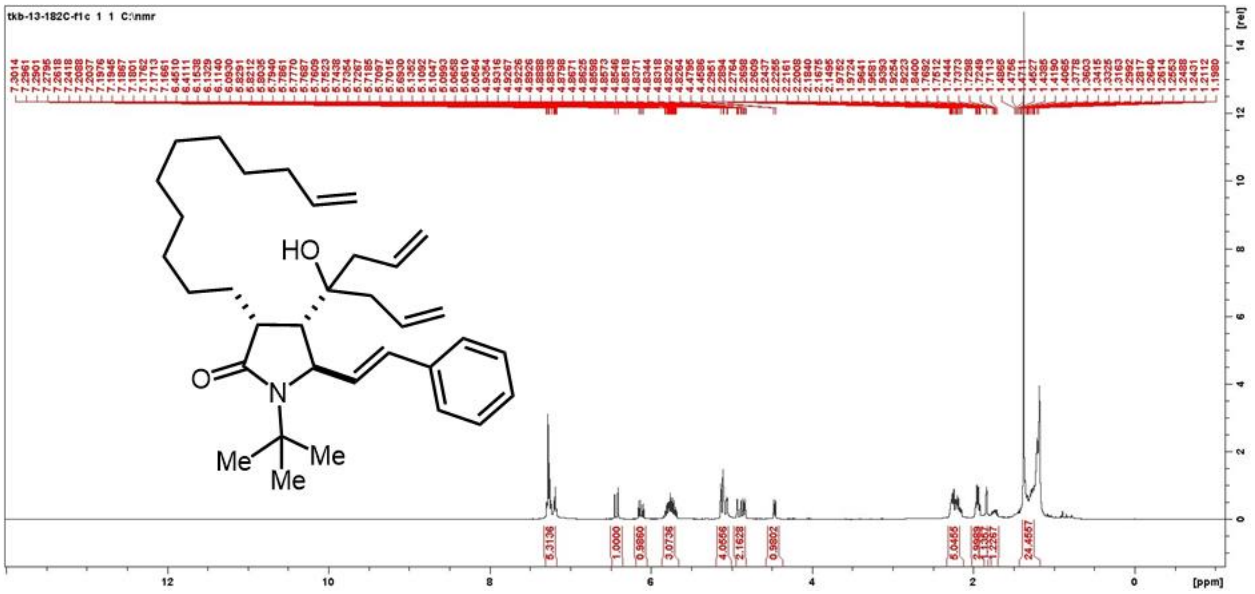


8t; 68%, 95:5 dr

E^+ = 11-bromoundecene

Compound 8t

Prepared in 0.50 mmol scale using **General Procedures C** and **D**. Grignard reagent = allylmagnesium bromide and electrophile = 11-bromoundecene. Purification: Flash chromatography on silica eluting with hexane/acetone (95:5 to 85:15). Yellowish oil. Yield = 172.0 mg, 68%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.16 (m, 5H), 6.43 (d, *J* = 16.0 Hz, 1H), 6.12 (dd, *J* = 15.9, 8.4 Hz, 1H), 5.87 – 5.65 (m, 3H), 5.16 – 5.07 (m, 3H), 5.06 (dt, *J* = 4.0, 1.7 Hz, 1H), 4.91 (dp, *J* = 17.1, 1.6 Hz, 1H), 4.84 (ddt, *J* = 10.2, 2.3, 1.3 Hz, 1H), 4.47 (d, *J* = 8.3 Hz, 1H), 2.34 – 2.13 (m, 5H), 1.96 (tdd, *J* = 6.5, 5.3, 4.0 Hz, 2H), 1.94 – 1.79 (m, 1H), 1.74 (ddt, *J* = 12.7, 10.5, 5.5 Hz, 1H), 1.48 – 1.19 (m, 24H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.98, 139.23, 136.49, 134.30, 133.03, 132.92, 129.95, 128.72, 127.85, 126.32, 120.06, 119.71, 114.09, 74.89, 60.92, 54.98, 52.18, 44.98, 40.84, 40.20, 33.80, 29.68, 29.55, 29.47, 29.12, 28.94, 28.36, 27.72. **HRMS-EI**$^+$ (*m/z*): calc for $C_{34}H_{51}NO_2$ $[M]^+$ 505.3920, found 505.3926.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Me
Me
Me
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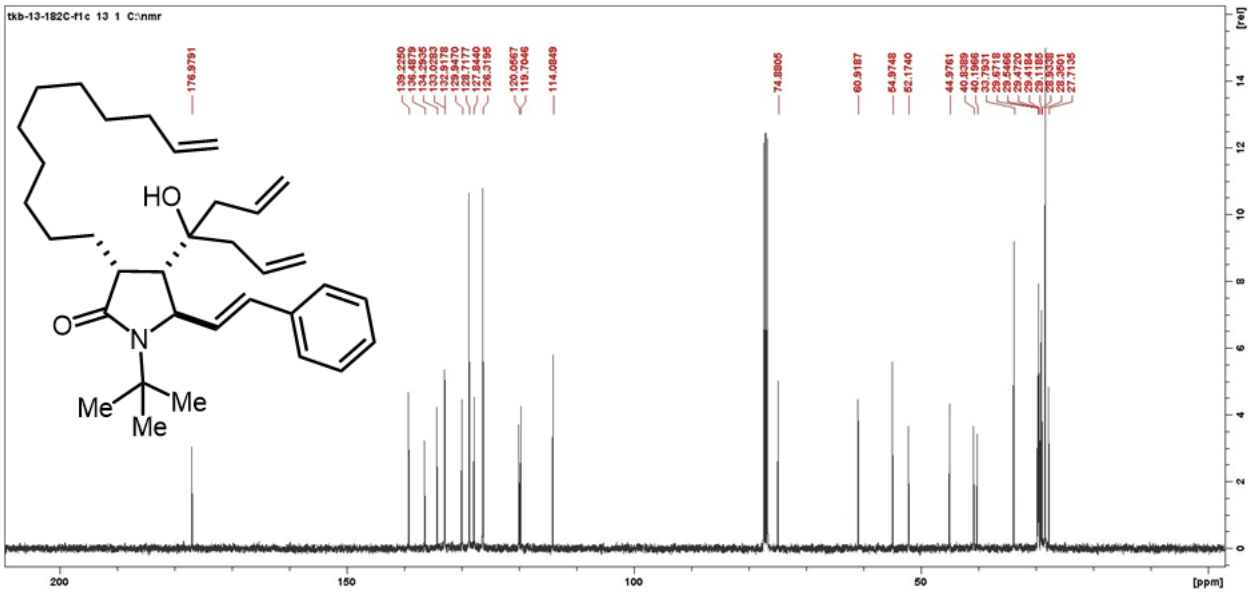
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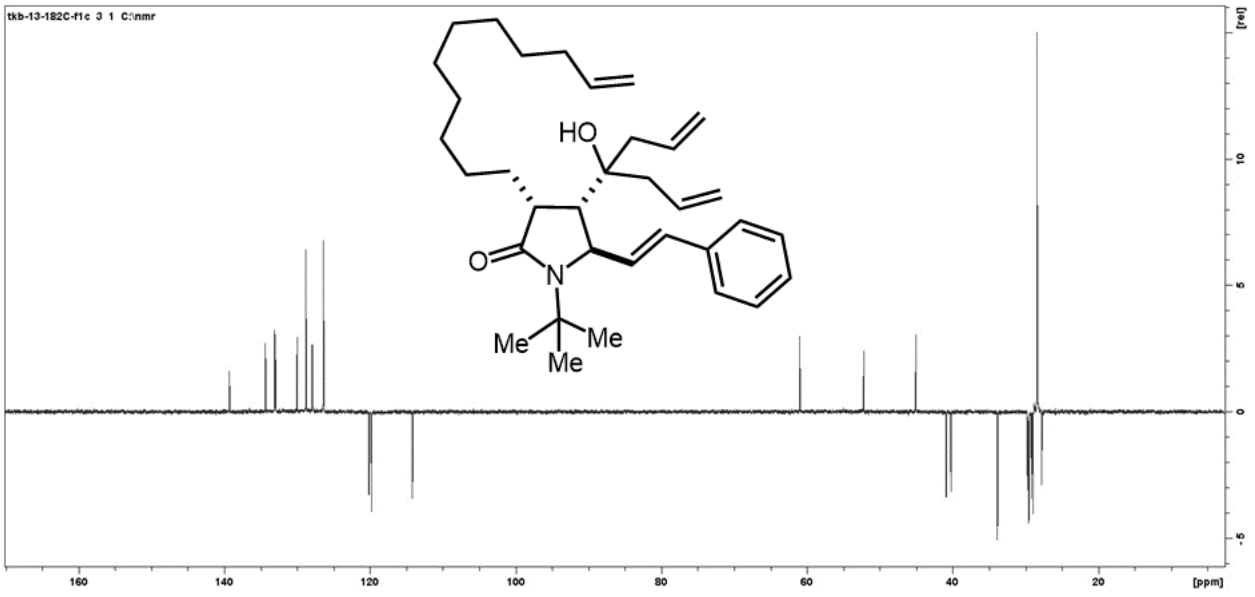
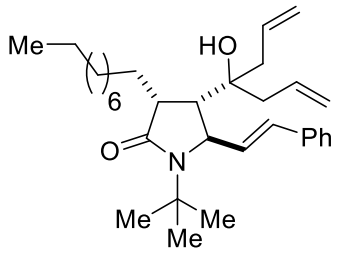
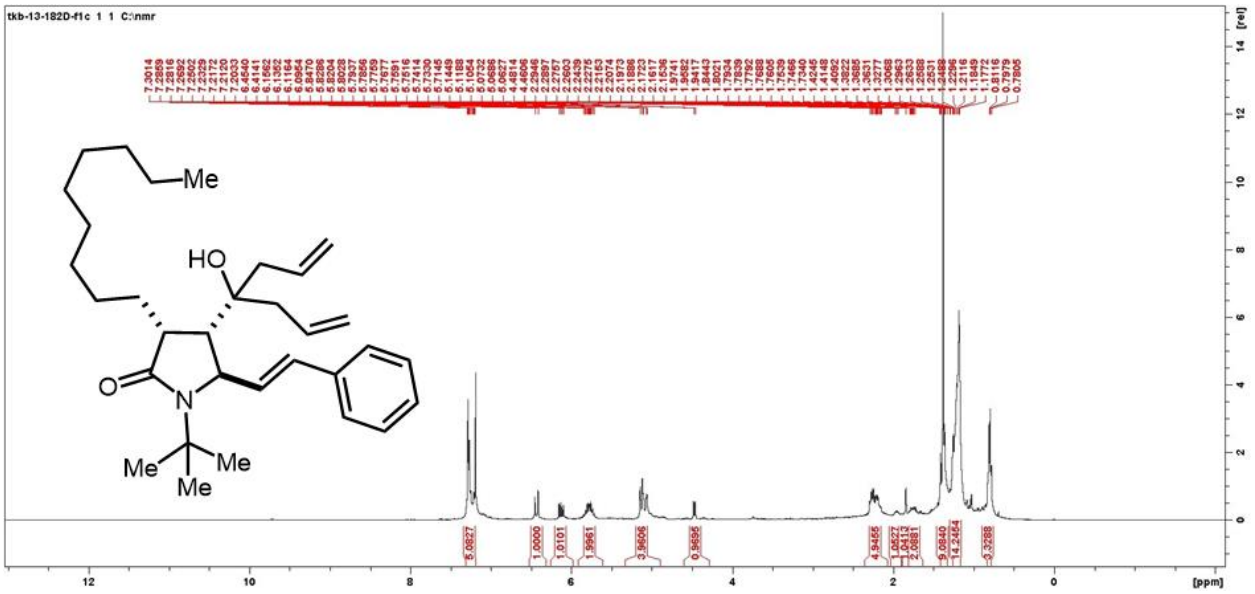




8u; 72%, 97:3 dr
E^+ = 1-bromononane

Compound 8u

Prepared in 0.50 mmol scale using **General Procedures C** and **D**. Grignard reagent = allylmagnesium bromide and electrophile = 1-bromononane. Purification: Flash chromatography on silica eluting with hexane/acetone (95:5 to 85:15). Yellowish oil. Yield = 172.7 mg, 72%, 97:3 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 – 7.19 (m, 5H), 6.43 (d, *J* = 16.0 Hz, 1H), 6.12 (dd, *J* = 15.9, 8.4 Hz, 1H), 5.84 – 5.69 (m, 2H), 5.16 – 5.04 (m, 4H), 4.47 (d, *J* = 8.3 Hz, 1H), 2.34 – 2.13 (m, 5H), 1.95 – 1.72 (m, 5H), 1.49 (h, *J* = 6.7 Hz, 2H), 1.38 (s, 9H), 1.27 – 1.16 (m, 17H), 0.79 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 177.17, 136.44, 134.10, 132.95, 132.86, 130.07, 128.73, 127.89, 126.33, 120.12, 119.78, 74.87, 63.08, 61.09, 55.17, 52.16, 44.97, 40.82, 40.16, 33.76, 32.82, 31.88, 29.68, 29.57, 29.49, 29.44, 29.31, 29.25, 28.33, 27.72, 25.75, 22.66, 14.09. **HRMS-EI$^+$** (*m/z*): calc for $C_{32}H_{49}NO_2$ $[M]^+$ 479.3763, found 479.3767.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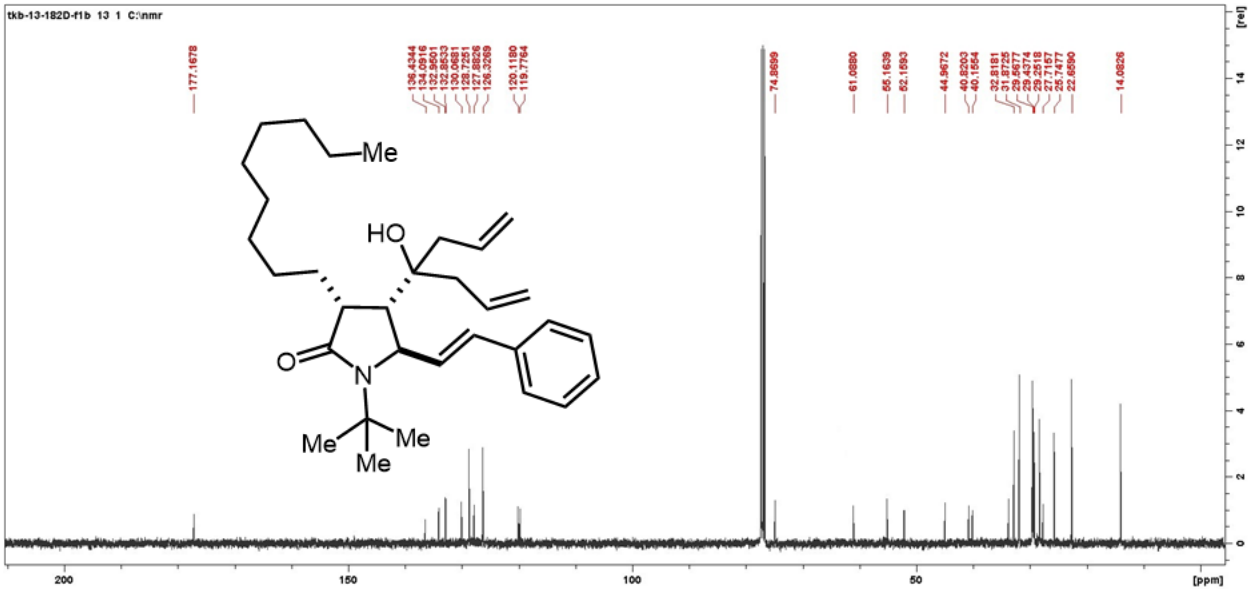
Me
HO
O
N
Me
Me
Me
[ppm]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130.0931
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127.8826
126.3269
120.1180
118.7764
74.8699
61.0890
55.1639
52.1693
44.9672
40.8203
40.1554
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29.4577
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Me
Me
Me
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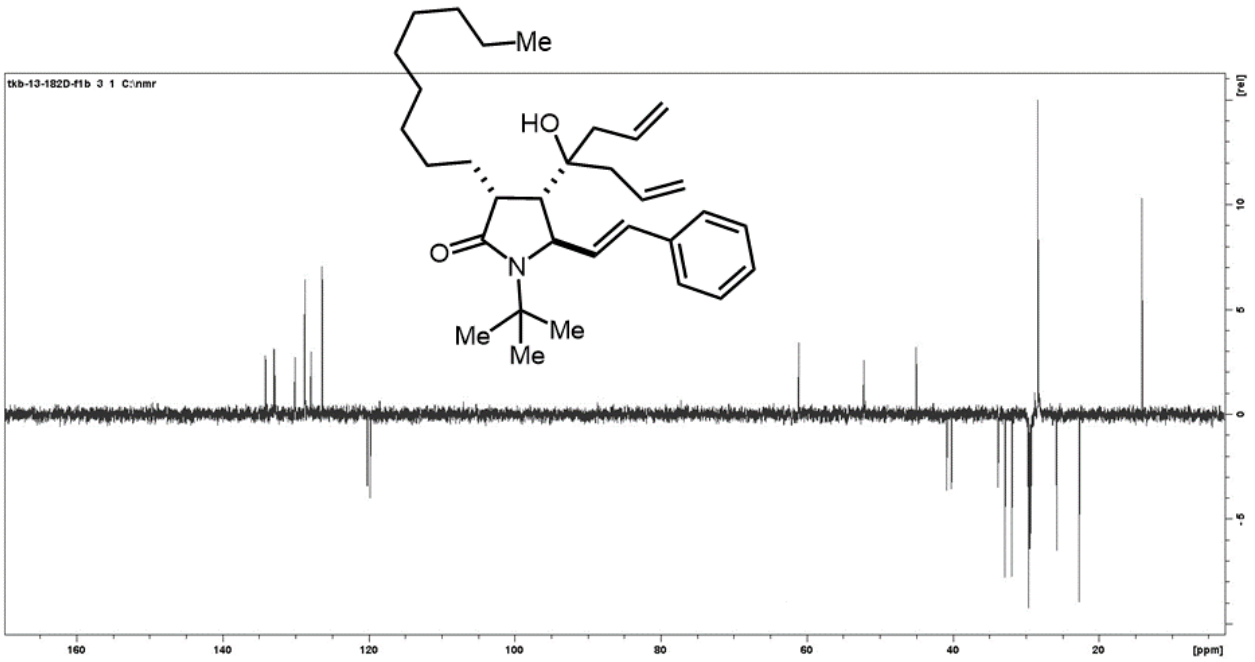
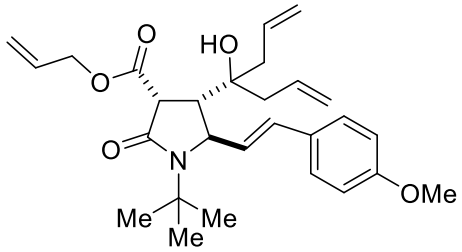


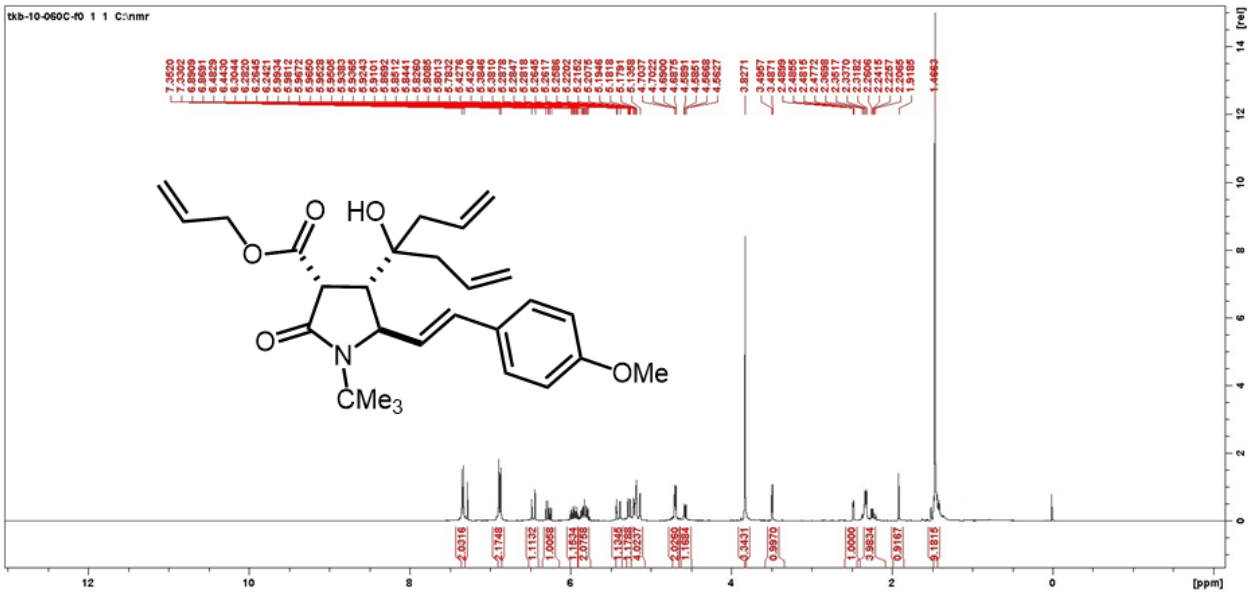


8v; 82%, 95:5 dr

E^+ = allyl chloroformate

Compound 8v

Prepared in 0.50 mmol scale using **General Procedures C** and **D**. Grignard reagent = allylmagnesium bromide and electrophile = allyl chloroformate. Purification: Flash chromatography on silica eluting with hexane/acetone (95:5 to 50:50). Yellowish oil. Yield = 191.7 mg, 82%, 95:5 dr. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.34 (d, *J* = 8.2 Hz, 2H), 6.89 (d, *J* = 8.2 Hz, 2H), 6.46 (d, *J* = 16.0 Hz, 1H), 6.27 (dd, *J* = 16.0, 9.0 Hz, 1H), 6.03 – 5.74 (m, 3H), 5.40 (dq, *J* = 17.2, 1.5 Hz, 1H), 5.27 (dq, *J* = 10.4, 1.3 Hz, 1H), 5.24 – 5.15 (m, 3H), 5.14 (p, *J* = 1.5 Hz, 1H), 4.70 (dq, *J* = 5.7, 1.2 Hz, 2H), 4.58 (dd, *J* = 9.0, 1.8 Hz, 1H), 3.83 (s, 3H), 3.49 (d, *J* = 3.4 Hz, 1H), 2.48 (dd, *J* = 3.5, 1.8 Hz, 1H), 2.40 – 2.26 (m, 3H), 2.23 (dd, *J* = 14.0, 7.7 Hz, 1H), 1.92 (s, 1H), 1.47 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.48, 169.07, 159.56, 132.48, 132.41, 131.75, 131.18, 130.10, 129.14, 127.78, 120.41, 120.20, 118.75, 114.14, 74.95, 66.22, 61.64, 55.83, 55.41, 51.79, 49.58, 40.99, 40.32, 28.24. **HRMS-EI$^+$** (*m/z*): calc for $C_{28}H_{37}NO_5$ $[M]^+$ 467.2672, found 467.2679.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N
CMe3
OMe
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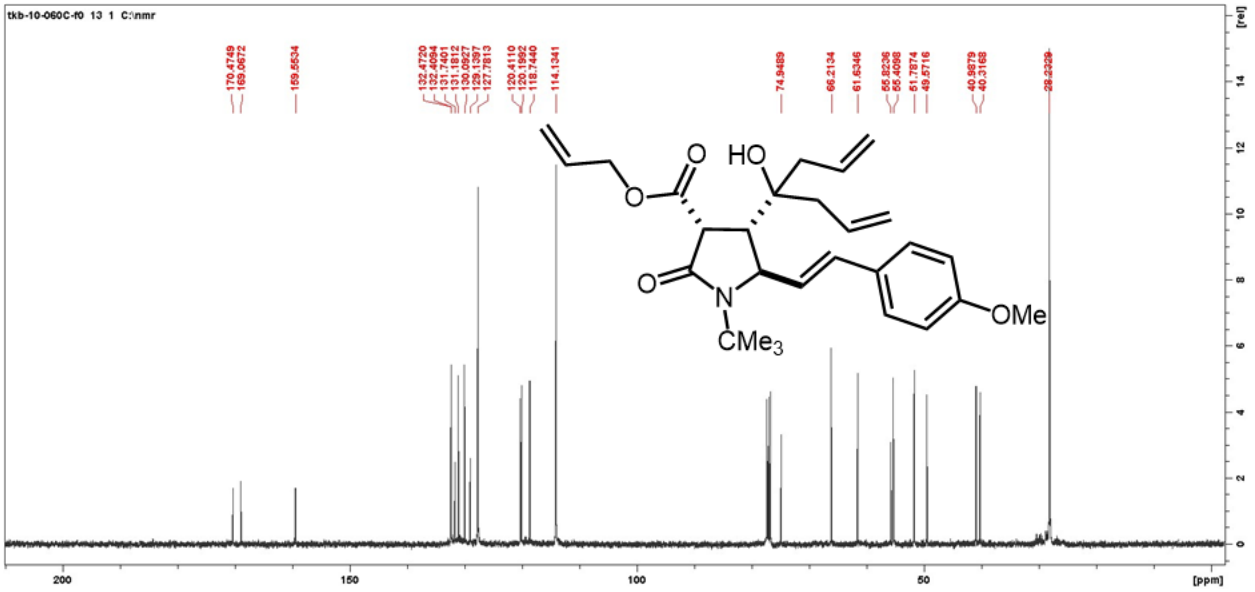
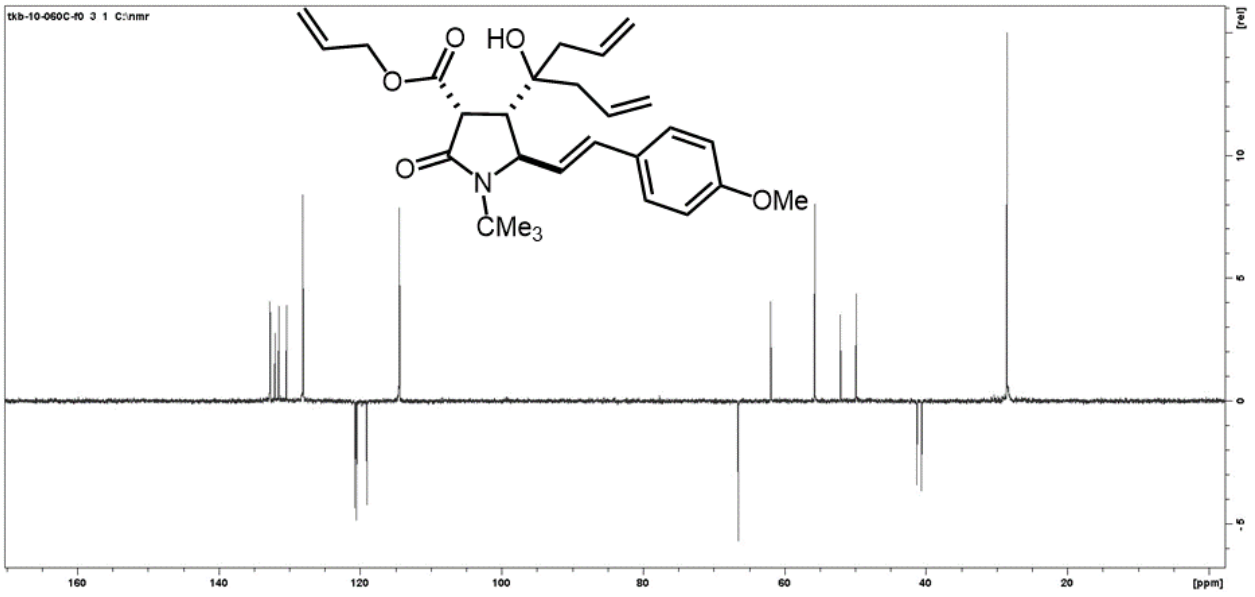
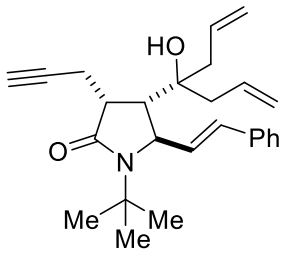
[rel]


tkb-10-060C-f0 13 1 C6nmr
HO
O
O
N
CMe3
OMe
[ppm]
[rel]



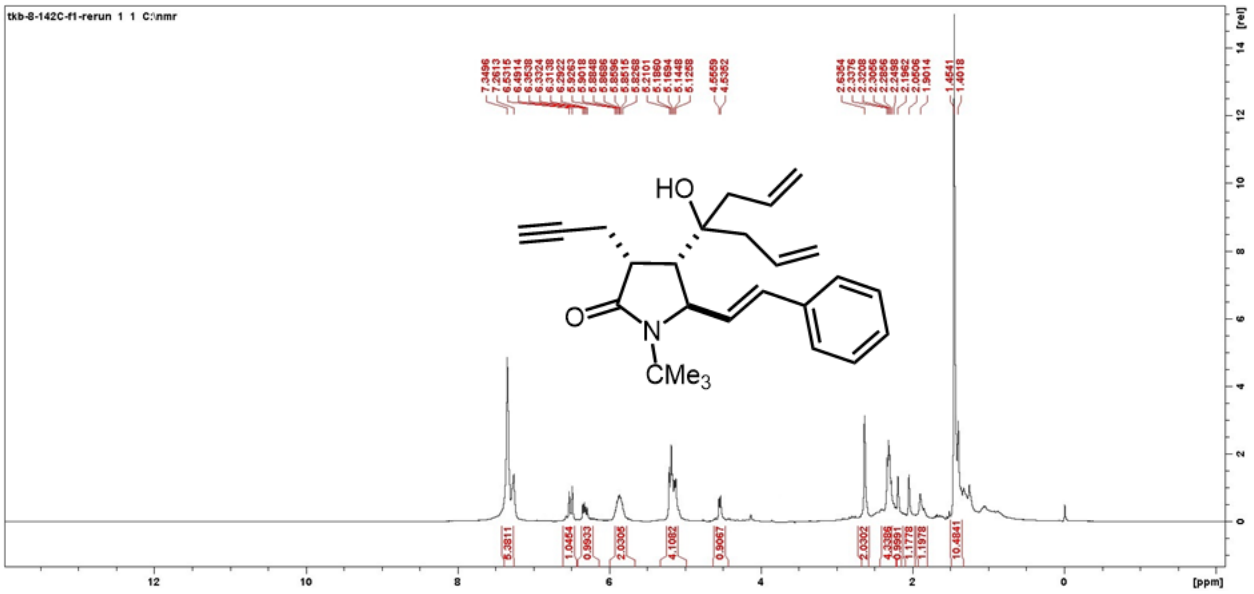


8w; 81%, 96:4 dr

E^+ = propargyl bromide

Compound 8w

Prepared in 0.50 mmol scale using **General Procedures C** and **D**. Grignard reagent = allylmagnesium bromide and electrophile = propargyl bromide. Purification: Flash chromatography on silica eluting with hexane/acetone (95:5 to 70:30). Yellowish oil. Yield = 158.6 mg, 81%, 96:4 dr. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.43 – 7.30 (m, 5H), 6.51 (d, *J* = 16.1 Hz, 1H), 6.32 (dd, *J* = 16.1, 8.7 Hz, 1H), 5.88 (dp, *J* = 17.2, 8.7, 7.5 Hz, 2H), 5.21 – 5.12 (m, 4H), 4.55 (d, *J* = 8.7 Hz, 1H), 2.64 (s, 2H), 2.34 – 2.28 (m, 4H), 2.20 (s, 1H), 2.05 (s, 1H), 1.90 (s, 1H), 1.45 (s, 9H), 1.38 – 1.21 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.51, 136.47, 134.34, 130.21, 128.81, 127.98, 126.42, 120.15, 120.00, 82.42, 74.80, 70.63, 55.45, 50.32, 43.65, 40.82, 40.38, 28.34, 22.22. **HRMS-EI$^+$** (*m/z*): calc for $C_{26}H_{33}NO_2$ $[M]^+$ 391.2511, found 391.2516.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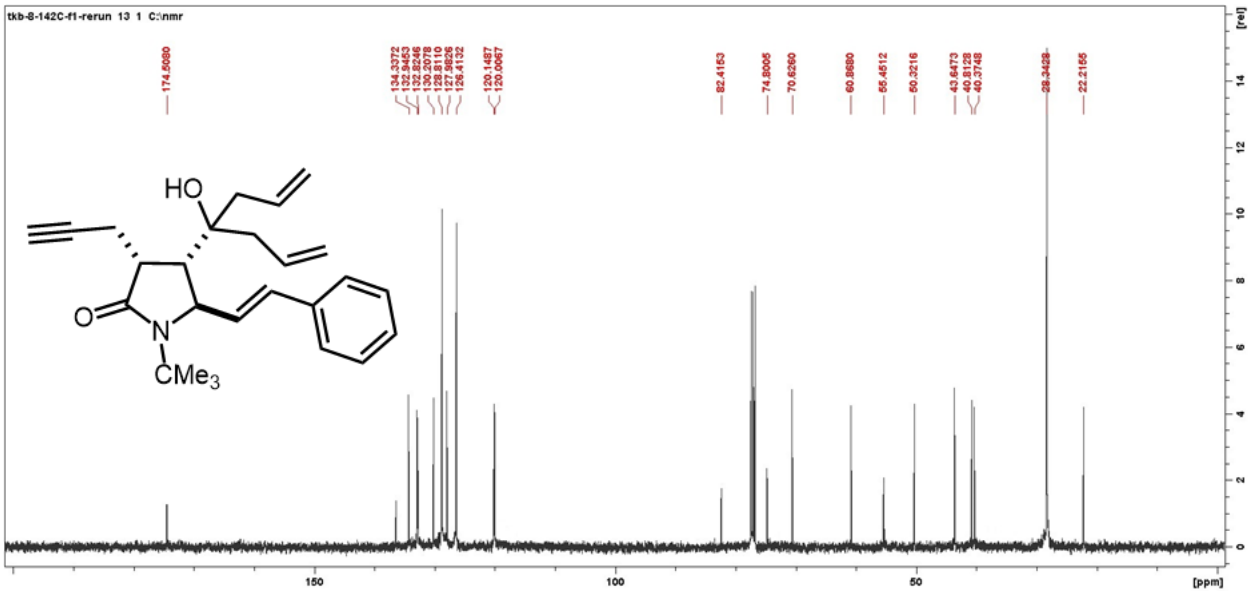
[rel]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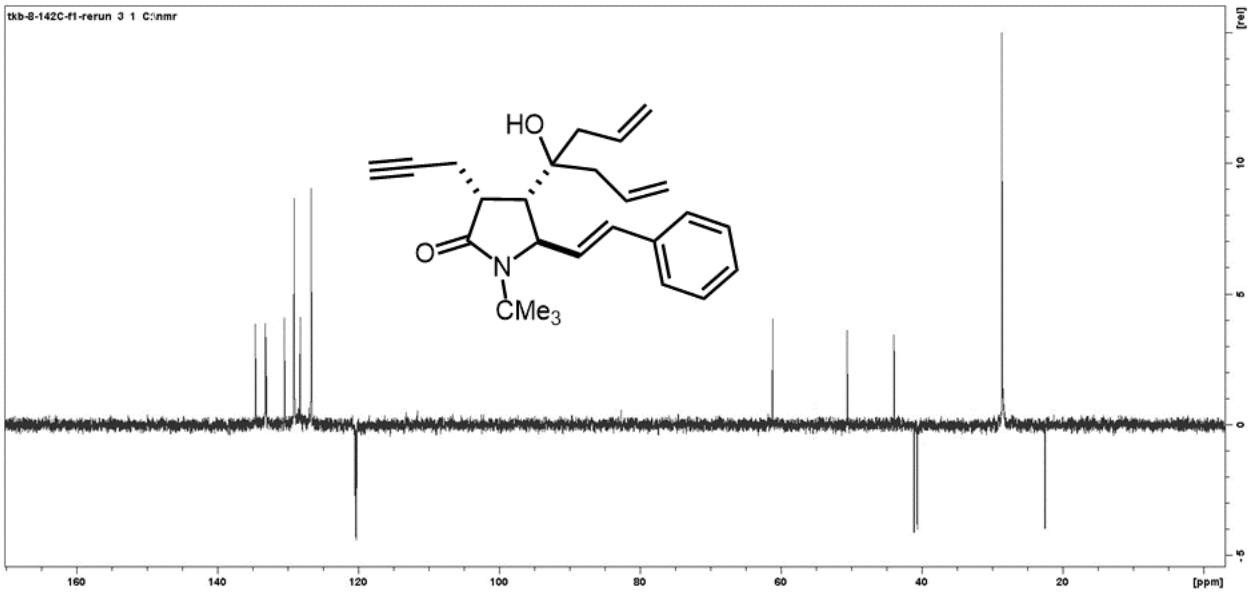
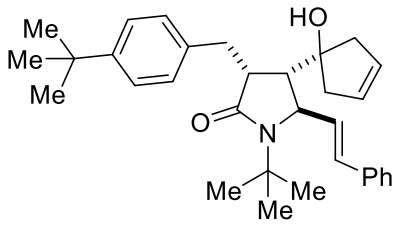


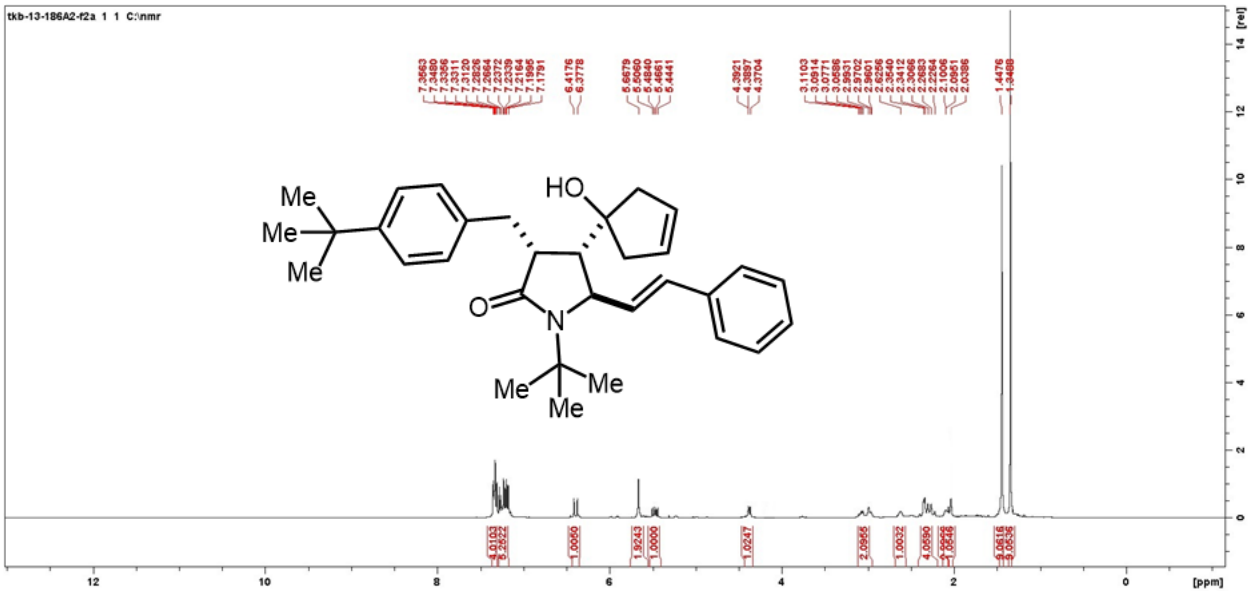


8x; 86%, 95:5 dr

E^+ = 4-*tert*-butylbenzyl bromide

Compound 8x

Prepared in 0.50 mmol scale using **General Procedures C** and **D**. Grignard reagent = allylmagnesium bromide then RCM and electrophile = 4-*tert*-butylbenzyl bromide. Purification: Flash chromatography on silica eluting with hexane/acetone (95:5 to 80:20). Yellowish oil. Yield = 202.8 mg, 86%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.13 (m, 9H), 6.40 (d, *J* = 15.9 Hz, 1H), 5.67 (s, 2H), 5.48 (dd, *J* = 16.0, 8.8 Hz, 1H), 4.38 (dd, *J* = 8.7, 1.9 Hz, 1H), 3.08 (dd, *J* = 13.4, 7.5 Hz, 1H), 2.98 (dd, *J* = 13.1, 4.3 Hz, 1H), 2.63 (s, 1H), 2.50 (s, 1H), 2.42 – 2.32 (m, 4H), 2.13 – 2.07 (m, 1H), 2.04 (t, *J* = 2.4 Hz, 1H), 1.45 (s, 9H), 1.35 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.93, 149.53, 136.45, 135.76, 134.36, 129.86, 129.80, 128.64, 128.60, 127.74, 126.38, 126.36, 125.31, 82.91, 62.60, 55.33, 50.33, 47.78, 45.21, 37.68, 34.45, 31.43, 28.37. **HRMS-EI$^+$** (*m/z*): calc for $C_{32}H_{41}NO_2$ $[M]^+$ 471.3137, found 471.3132.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O
N
Me
Me
Me
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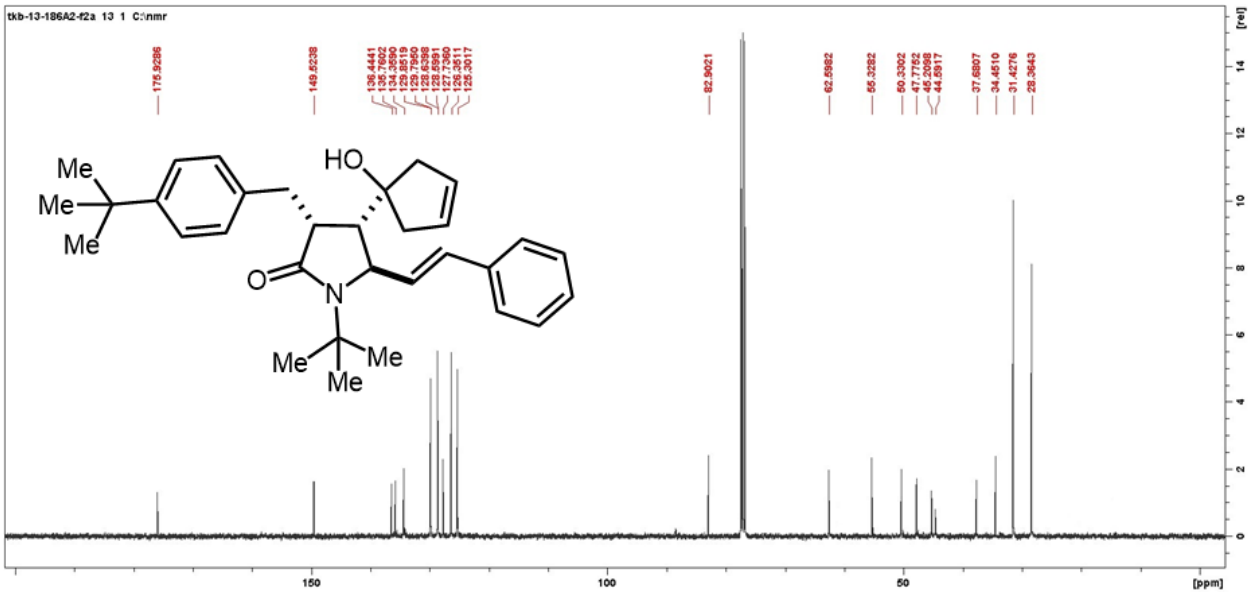
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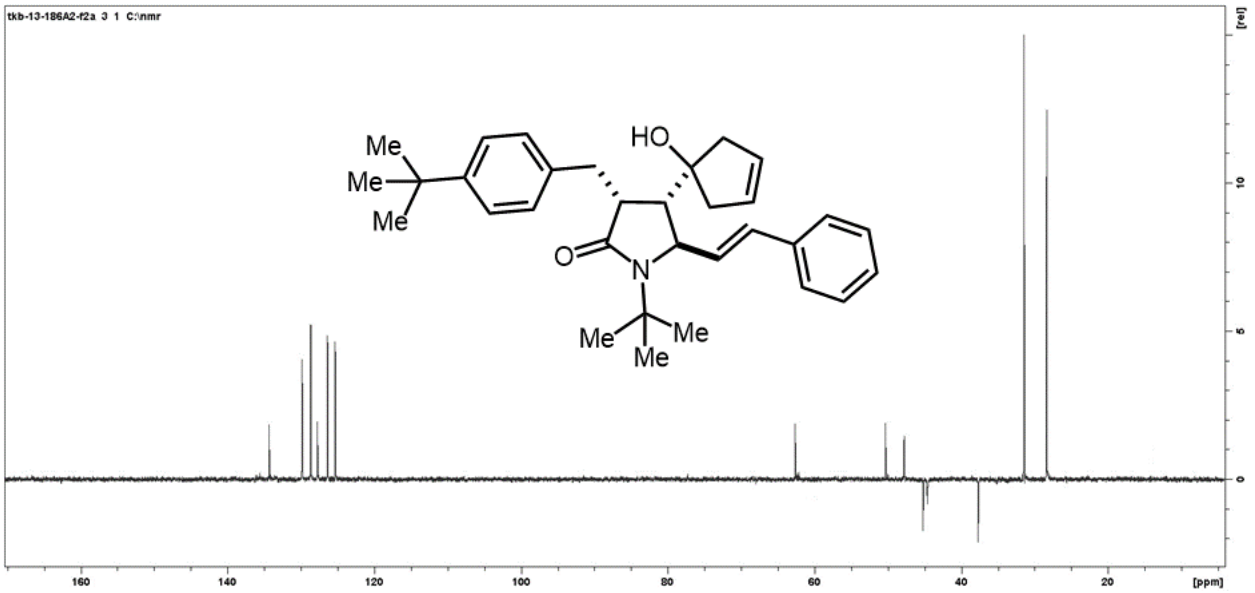
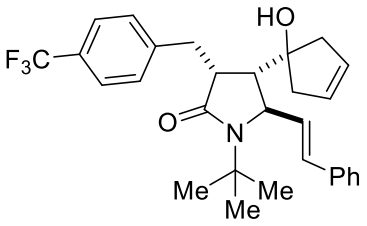


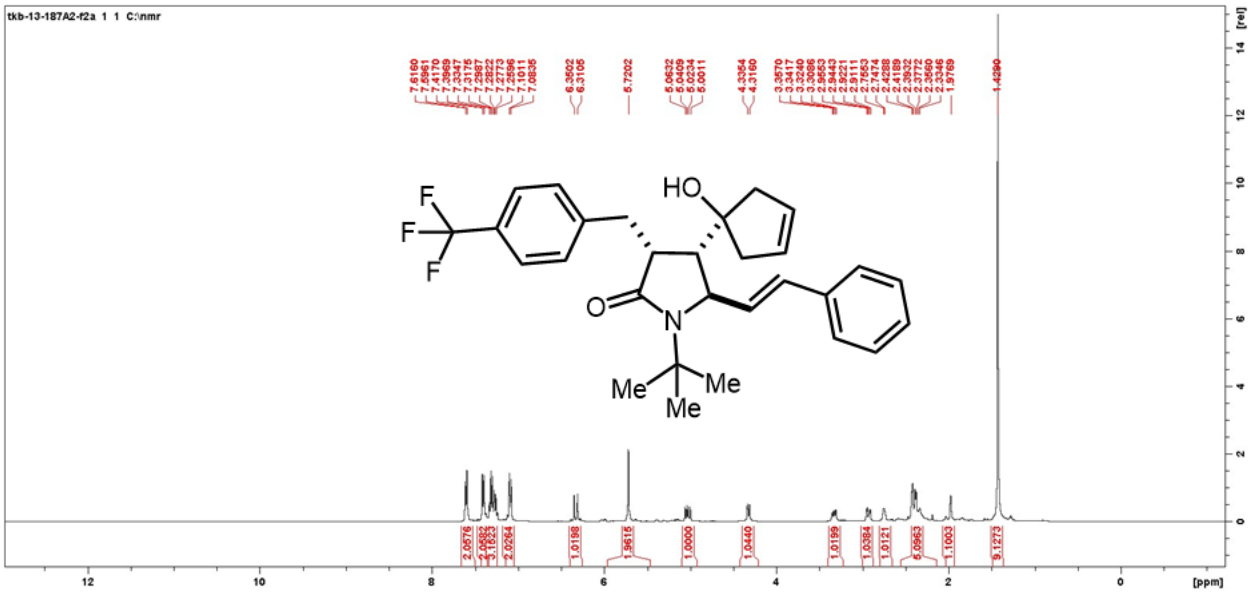


8y; 86%, 95:5 dr

E^+ = 4-trifluoromethylbenzyl bromide

Compound 8y

Prepared in 0.50 mmol scale using **General Procedures C** and **D**. Grignard reagent = allylmagnesium bromide then RCM and electrophile = 4-trifluoromethylbenzyl bromide. Purification: Flash chromatography on silica eluting with hexane/acetone (95:5 to 80:20). Yellowish oil. Yield = 207.9 mg, 86%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, *J* = 7.8 Hz, 2H), 7.41 (d, *J* = 8.0 Hz, 2H), 7.32 (dd, *J* = 8.1, 6.3 Hz, 2H), 7.30 – 7.22 (m, 1H), 7.15 – 7.05 (m, 2H), 6.41 – 6.25 (m, 1H), 5.72 (s, 2H), 5.09 – 4.97 (m, 1H), 4.33 (dd, *J* = 8.9, 2.0 Hz, 1H), 3.33 (dd, *J* = 13.3, 6.2 Hz, 1H), 2.93 (dd, *J* = 13.3, 4.6 Hz, 1H), 2.79 – 2.71 (m, 1H), 2.50 – 2.33 (m, 5H), 1.98 (dd, *J* = 3.4, 2.0 Hz, 1H), 1.43 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.35, 143.13, 135.99, 133.57, 130.78, 130.73, 129.95, 129.27, 128.95, 128.70, 128.67, 128.64, 128.62, 127.93, 126.22, 126.18, 125.66, 125.38, 125.34, 125.30, 122.96, 82.82, 62.40, 55.48, 50.10, 47.21, 45.22, 44.81, 37.63, 28.29. **HRMS-EI$^+$** (*m/z*): calc for $C_{29}H_{32}F_3NO_2$ $[M]^+$ 483.2385, found 483.2383.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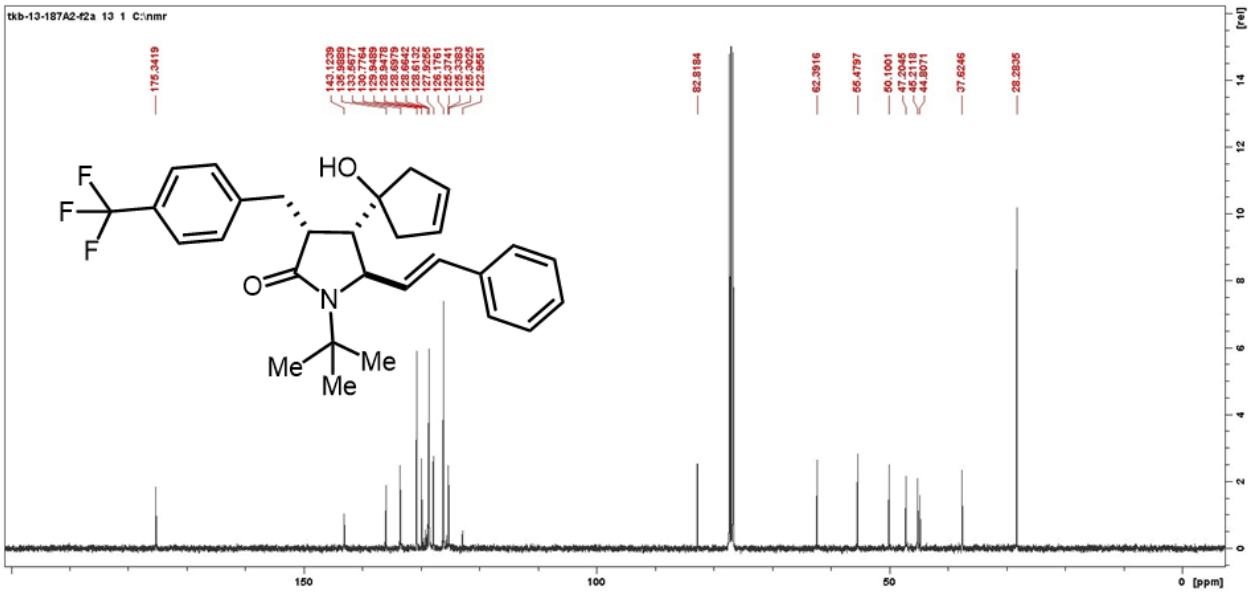
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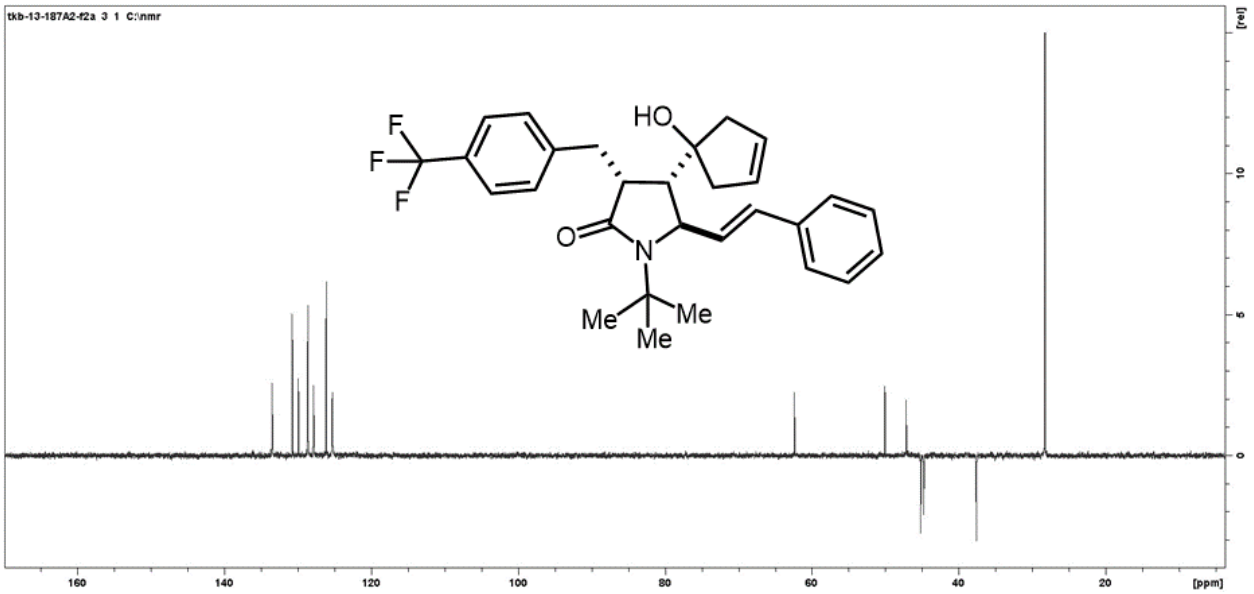
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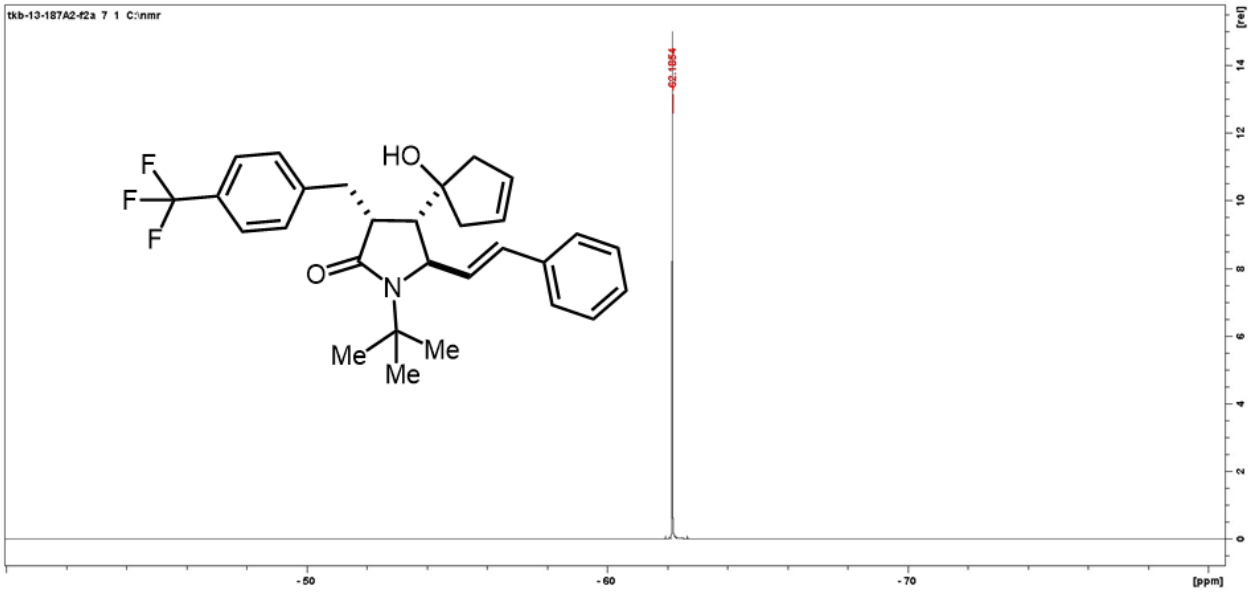
[rel]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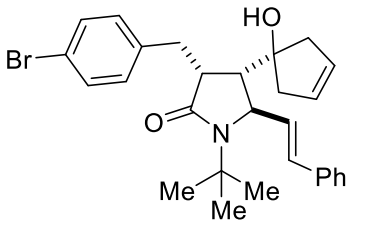
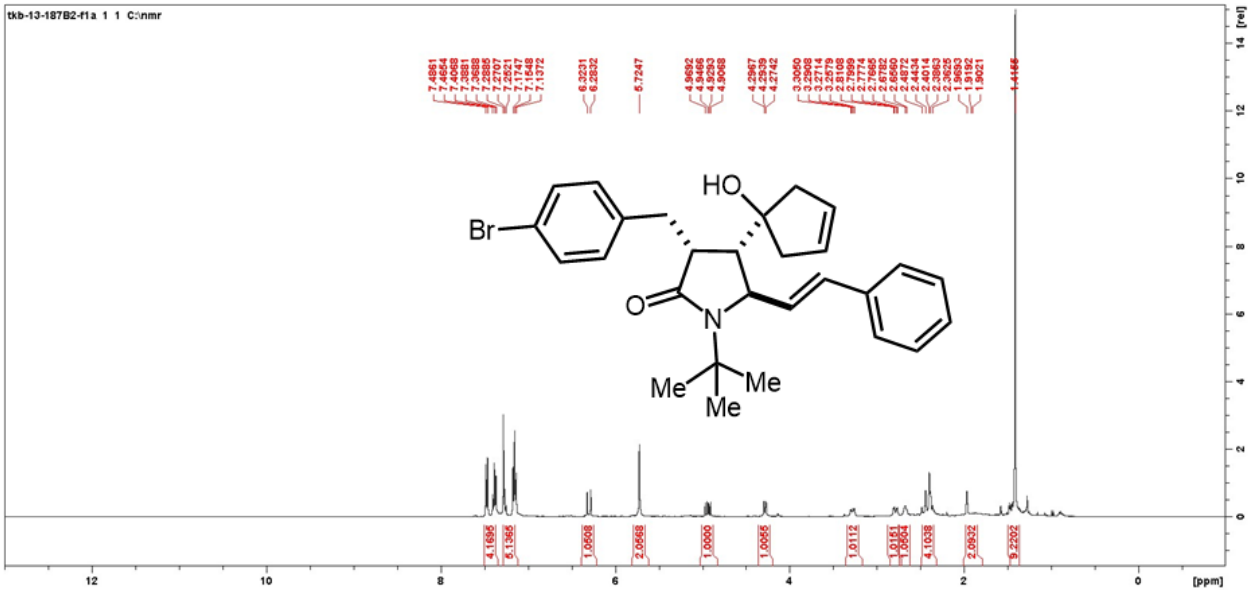
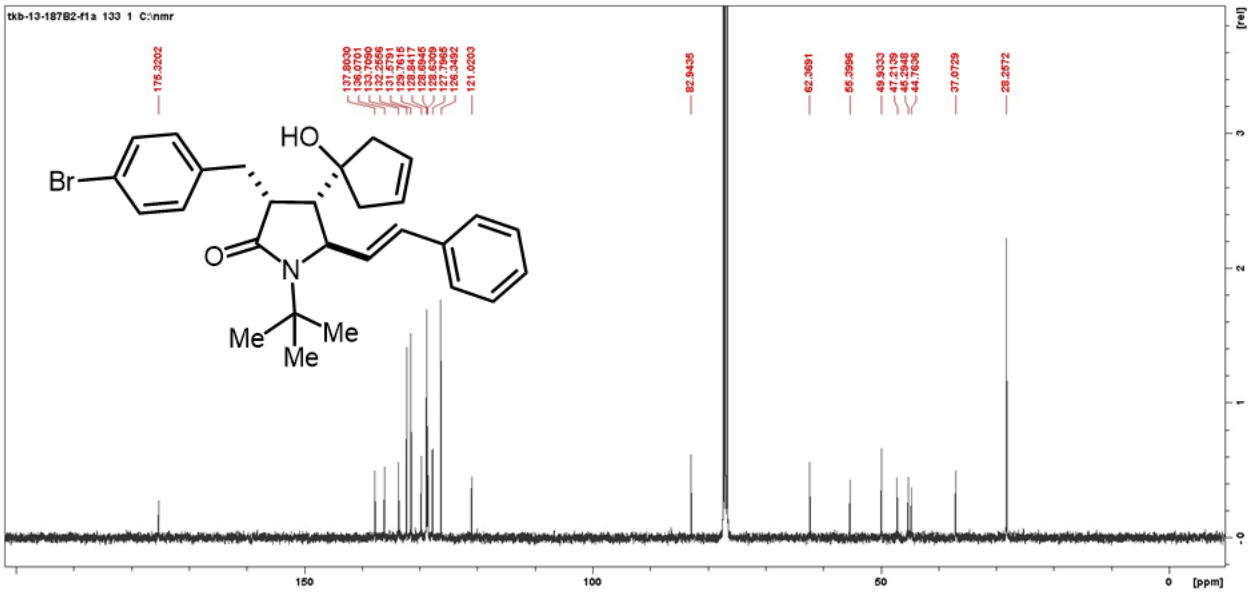


8z; 83%, 95:5 dr
E^+ = 4-bromobenzyl bromide

Compound 8z

Prepared in 0.50 mmol scale using **General Procedures C** and **D**. Grignard reagent = allylmagnesium bromide then RCM and electrophile = 4-bromobenzyl bromide. Purification: Flash chromatography on silica eluting with hexane/acetone (95:5 to 80:20). Yellowish oil. Yield = 205.2 mg, 83%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 – 7.43 (m, 2H), 7.39 (t, *J* = 7.6 Hz, 3H), 7.32 – 7.23 (m, 1H), 7.20 – 7.07 (m, 3H), 6.30 (d, *J* = 15.9 Hz, 1H), 5.73 (s, 2H), 4.94 (dd, *J* = 16.0, 9.0 Hz, 1H), 4.28 (dd, *J* = 9.1, 2.0 Hz, 1H), 3.28 (dd, *J* = 13.3, 5.6 Hz, 1H), 2.79 (dd, *J* = 13.4, 4.6 Hz, 1H), 2.68 (s, 1H), 2.42 – 2.32 (m, 4H), 1.97 (dd, *J* = 3.4, 1.9 Hz, 1H), 1.42 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.32, 137.81, 136.07, 133.71, 132.26, 131.58, 129.77, 128.85, 128.70, 128.63, 127.80, 126.35, 121.03, 82.95, 62.37, 55.40, 49.94, 47.22, 45.30, 44.77, 37.08, 28.26. **HRMS-EI**$^+$ (*m/z*): calc for $C_{28}H_{32}BrNO_2$ $[M]^+$ 493.1616, found 493.1622.

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O
N
Me
Me
Me
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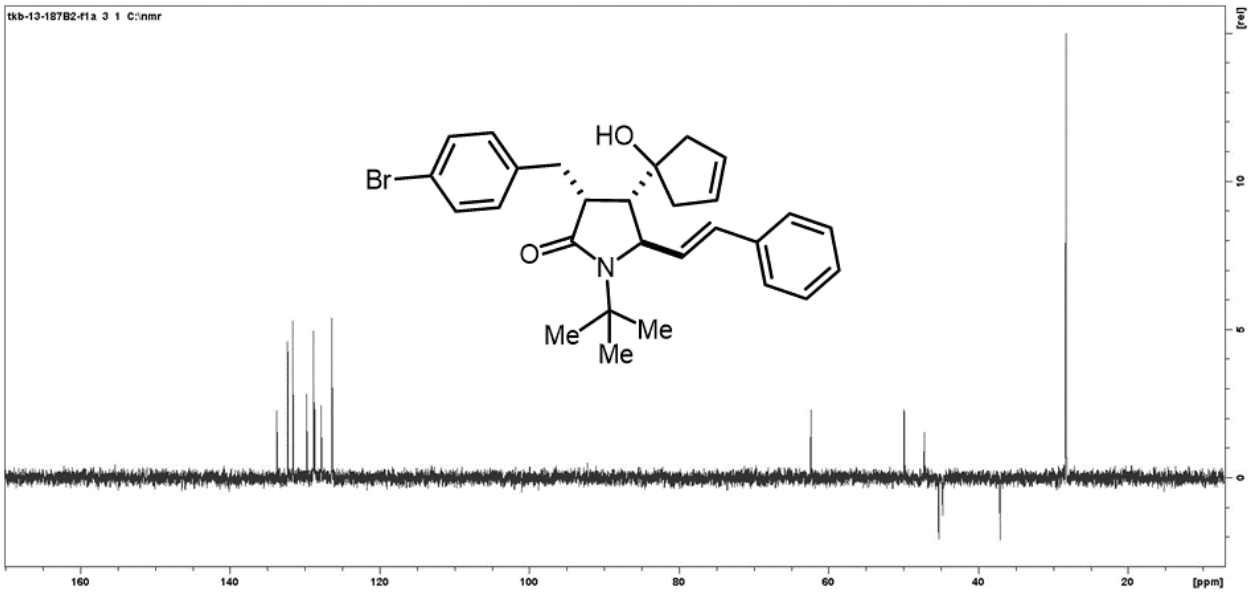
100
50
0
[ppm]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Br
O
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Me
Me
Me
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140
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80
60
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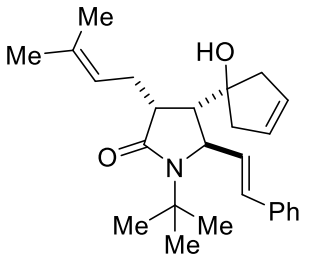
20
[ppm]

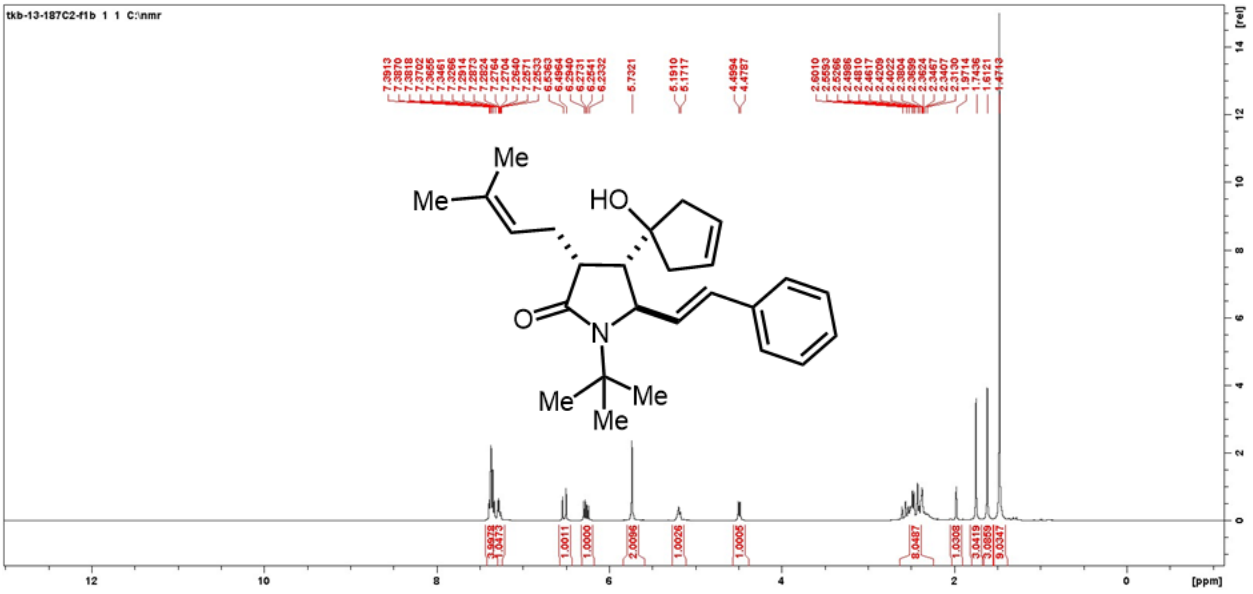


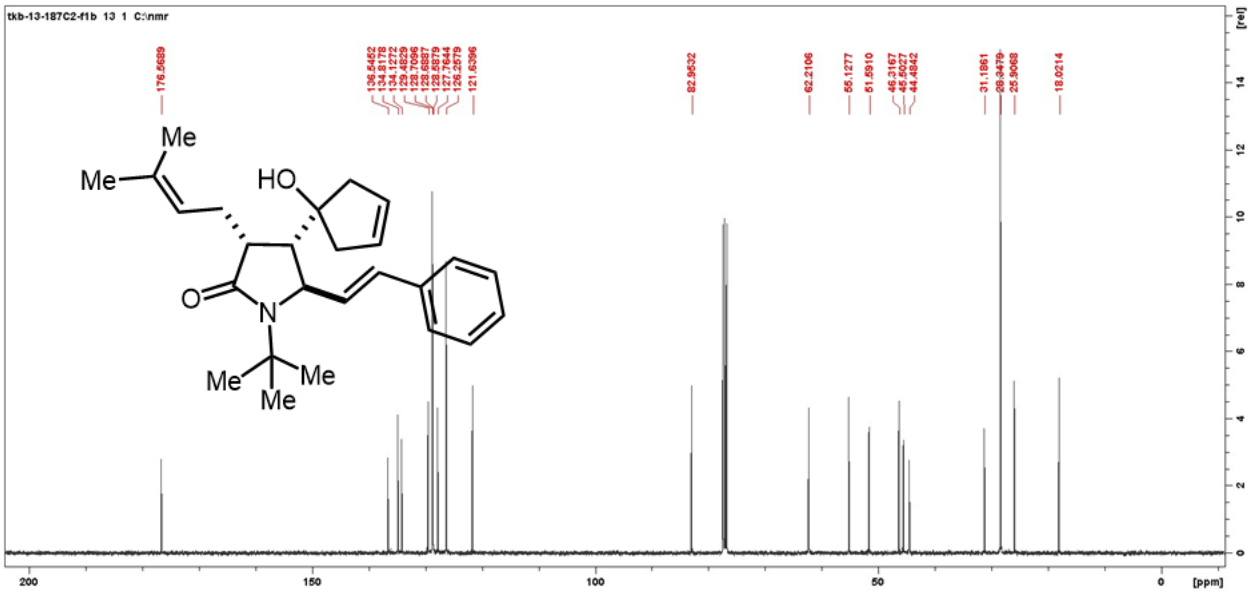
8z1; 84%, 95:5 dr

E^+ = prenyl bromide

Compound 8z1

Prepared in 0.50 mmol scale using **General Procedures C** and **D**. Grignard reagent = allylmagnesium bromide then RCM and electrophile = prenyl bromide. Purification: Flash chromatography on silica eluting with hexane/acetone (95:5 to 80:20). Yellowish oil. Yield = 165.3 mg, 84%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.31 (m, 4H), 7.31 – 7.23 (m, 1H), 6.52 (d, *J* = 16.0 Hz, 1H), 6.26 (dd, *J* = 15.9, 8.4 Hz, 1H), 5.73 (s, 2H), 5.19 (ddd, *J* = 8.9, 3.8, 2.0 Hz, 1H), 4.49 (dd, *J* = 8.4, 1.7 Hz, 1H), 2.58 – 2.48 (m, 8H), 1.97 (d, *J* = 2.0 Hz, 1H), 1.74 (d, *J* = 1.3 Hz, 3H), 1.61 (d, *J* = 1.3 Hz, 3H), 1.47 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.57, 136.55, 134.82, 134.13, 129.49, 128.72, 128.69, 128.59, 127.77, 126.26, 121.64, 82.96, 62.21, 55.13, 51.59, 46.32, 45.51, 44.49, 31.19, 28.35, 25.91, 18.02. **HRMS-EI**$^+$ (*m/z*): calc for $C_{26}H_{35}NO_2$ $[M]^+$ 393.2668, found 393.2674.

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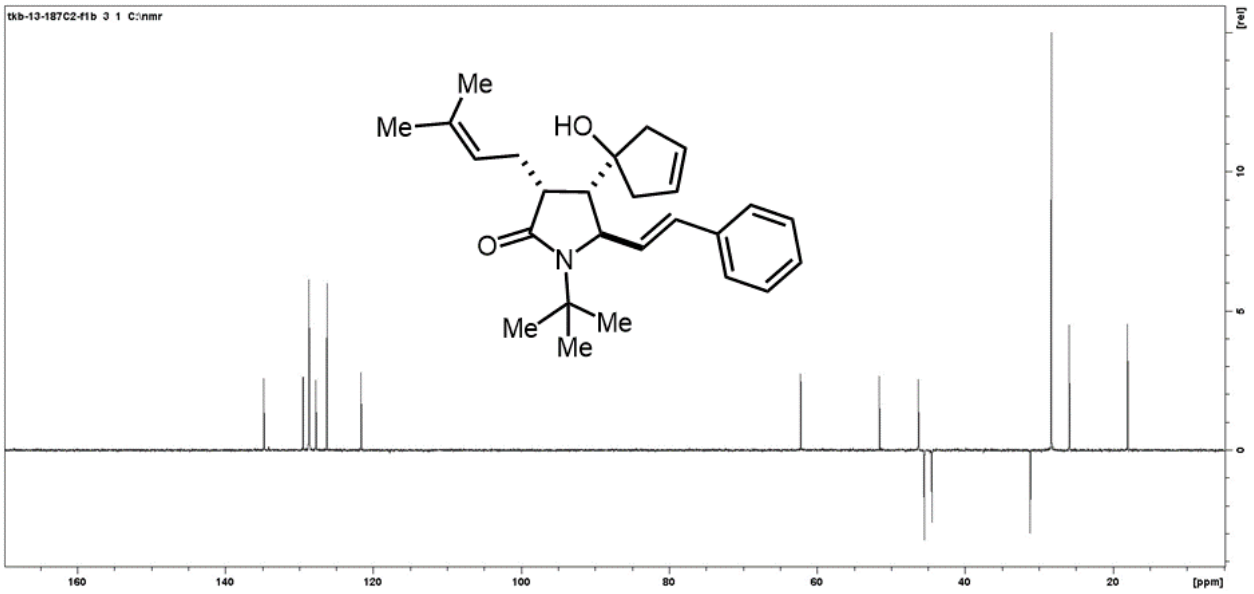
50
0
[ppm]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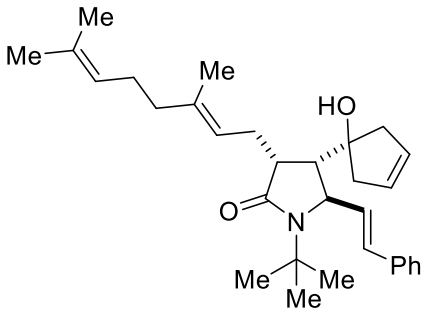
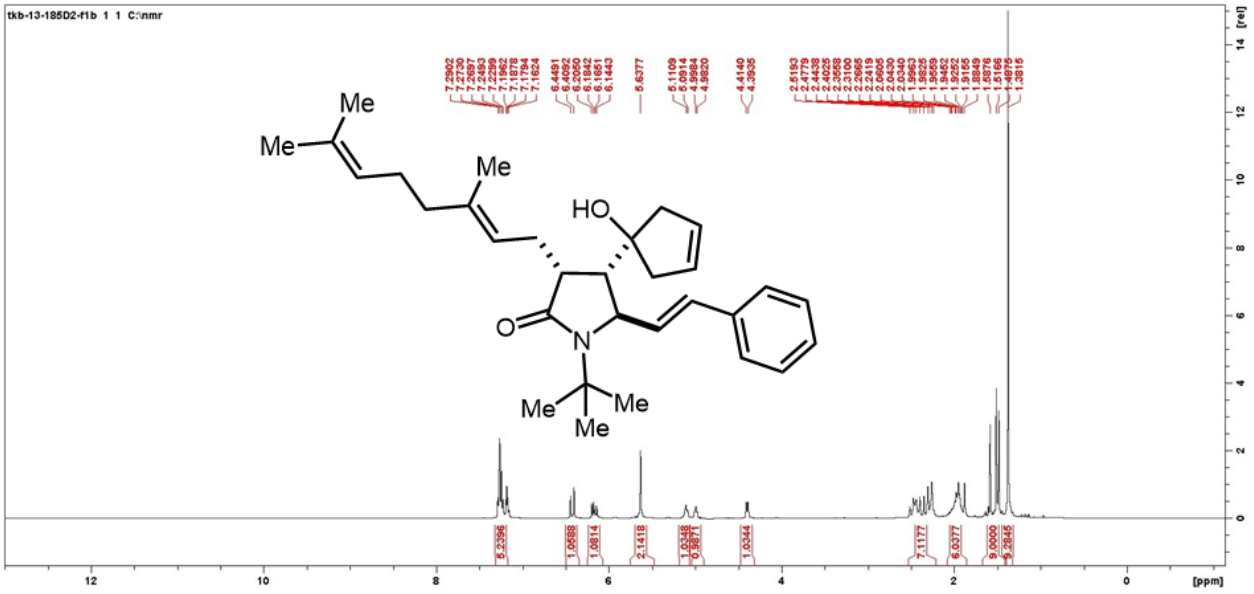


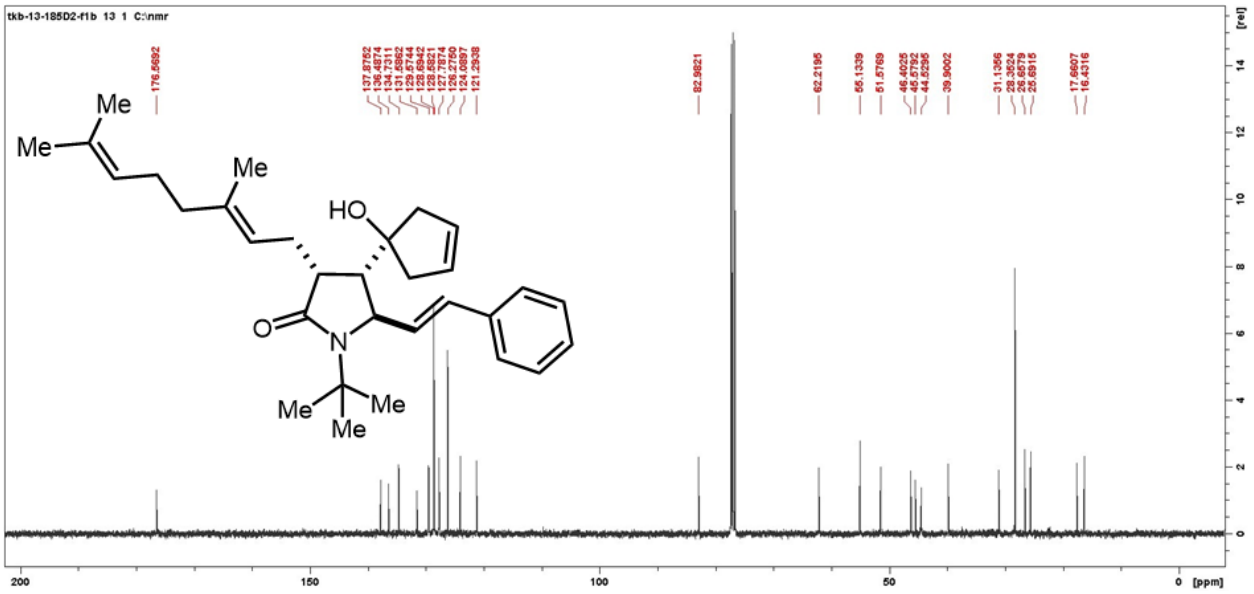
8z2; 81%, 95:5 dr

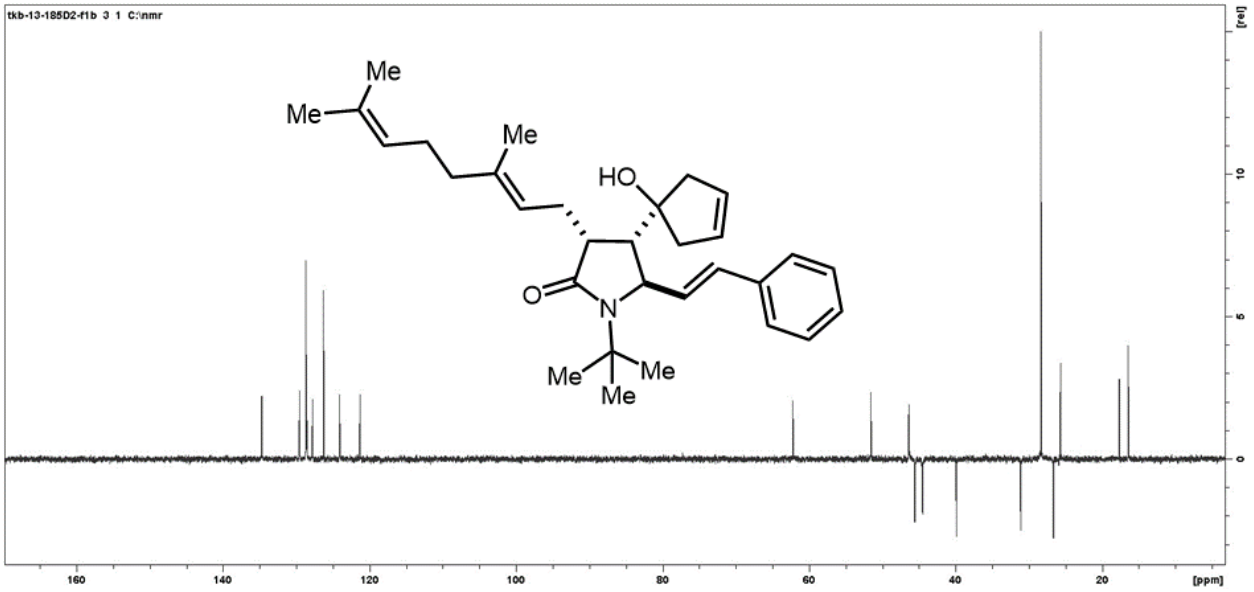
E^+ = geranyl bromide

Compound 8z2

Prepared in 0.50 mmol scale using **General Procedures C** and **D**. Grignard reagent = allylmagnesium bromide then RCM and electrophile = geranyl bromide. Purification: Flash chromatography on silica eluting with hexane/acetone (95:5 to 80:20). Yellowish oil. Yield = 187.0 mg, 81%, 95:5 dr. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.16 (m, 5H), 6.43 (d, *J* = 16.0 Hz, 1H), 6.17 (dd, *J* = 16.0, 8.3 Hz, 1H), 5.64 (s, 2H), 5.10 (d, *J* = 8.9 Hz, 1H), 5.00 (tt, *J* = 6.6, 1.6 Hz, 1H), 4.44 – 4.36 (m, 1H), 2.54 – 1.89 (m, 7H), 1.59 (s, 3H), 1.57 (s, 3H), 1.49 (s, 3H), 1.38 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.57, 137.88, 136.49, 134.73, 131.59, 129.58, 128.72, 128.70, 128.67, 128.59, 127.79, 126.28, 124.09, 121.30, 82.99, 62.22, 55.14, 51.58, 46.41, 45.58, 44.53, 39.90, 31.14, 28.36, 26.66, 25.69, 17.66, 16.43. **HRMS-EI**$^+$ (*m/z*): calc for $C_{31}H_{43}NO_2$ $[M]^+$ 461.3294, found 461.3299.







References

References

(1) Braunstein, H.; Langevin, S.; Khim, M.; Adamson, J.; Hovenkotter, K.; Kotlarz, L.; Mansker, B.; Beng, T. K. *Org. Biomol. Chem.* **2016**, *14*, 8864.